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The Scale Influence Of Substituents In
Paraffine Monobasic Acids. The Phenyl Radical.

THE SCALE OF INFLUENCE OF SUBSTITUENTS IN PARAFFIN,
MONOBASIC ACIDS. THE PHENYL RADICAL.

BY

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THESIS

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I HEREBY RECOMMEND THAT THE THESIS PREPARED UNDER MY SUPER-
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THE SCALE OF INFLUENCE OF SUBSTITUENTS IN PARAFFIN
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I INTRODUCTION.

The development of a science proceeds thru two distinct phases. In the first place, a great number of detailed facts must be collected, which are later classified and correlated. When sufficient knowledge is available, laws are formulated, by means of which new facts can be foretold and behaviors predicted. However, it is often the case that hypotheses are founded upon insufficient data, or upon inaccurate observation. Thus the desire for a generalization is likely to prove too strong for the investigator.

When a science is in the first phase of its development it may be called descriptive. For example, Mineralogy is largely a descriptive science. On the other hand, Chemistry is well along in the second stage of its development. This is especially true of Organic Chemistry. For more than a hundred years the data have been accumulating - the hewn stones awaiting the builders. Since the time of the masters, Williamson and Kekulé and van't Hoff, the structure has taken shape. In fact, so much emphasis is placed on the side of theory, that at the present time, justly or unjustly, little recognition is likely to be given to the so called 'Synthetic Chemist'. All are seeking the fundamental laws. So much has been

gained in this direction, that now Organic Chemistry seems to be the most satisfactory of the sciences. At least it seems so to its devotees.

In an endeavor to contribute in a small way to the general knowledge of the subject, Derick and his students at the University of Illinois have, for the past few years, been studying the effect of one atom on the others in the molecule. Their attention has been directed particularly to the study of the influence of negative groups or atoms in the monobasic paraffin acids. The following thesis consists of a part of this research now being carried on. The effect of the substitution of the phenyl radical for hydrogen in the simple fatty acids will be considered.

II HISTORICAL.

The chemical properties of a compound depend mainly upon the two following factors:

- 1) The nature of the atoms, and
- 2) The mode of linking of the atoms.

Furthermore, the physical properties depend, to a marked extent, upon the molecular weight of the substance.

The Nature and Mode of Linking of the Atoms. Suppose, that in the compound, water, one of the hydrogen atoms is replaced by chlorine giving the compound, hypochlorous acid, HOCl . It will be found that the presence of the chlorine atom has decidedly affected the oxygen-hydrogen linkage. While water is a very weak acid, the substance, hypochlorous acid, is able to dissolve iron. Furthermore, the stability of the molecule has been greatly affected.

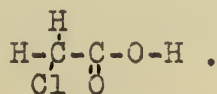
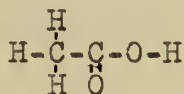
If, instead of chlorine, potassium be substituted for one of the hydrogen atoms of the water molecule, it will be observed that the resulting compound, potassium hydroxide, will present yet other differences in properties, due to the new substituent in the molecule. Considering the matter from the standpoint of the dissociation theory, one might say that in the first case the oxygen-hydrogen linkage has been weakened, while in the second case this linkage has been strengthened.

In these examples the important fact to consider is the nature of the atoms in the molecule. In general, in the field of Inorganic Chemistry this is the important consideration. Here when the analysis of a substance has been made the formula follows. On the other hand, the organic chemist has merely made a beginning

when the empirical formula of a compound has been deduced. Since a vast majority of the one-hundred-and-twenty thousand or more organic compounds are composed of the elements carbon, hydrogen, oxygen, and nitrogen; it is obvious that the structural formula - which is the short-hand expression of the chemical properties of the substance - must also be deduced. Thus, the molecular formula, C_2H_6O , might mean little to the chemist since it represents both the substance dimethyl ether and ethyl alcohol.

Our structural formulae are considered by many to represent not only the chemical properties of the compound, but also to indicate the relative positions of the atoms in the molecule. Much attention has been given to this side of Organic Chemistry. In this connection the theories of Kekulé and van't Hoff stand out pre-eminently. Of late years the same symbols have been used in the attempt to represent physical as well as chemical properties. If the formulae fail to express these properties it should be remembered that they were not designed for this purpose.

The van't Hoff Factors. Returning to the discussion of the influence of one atom upon another in the molecule, due to the specific nature of the atom, consider the two compounds, acetic acid and monochloroacetic acid,



Here the substitution of chlorine for hydrogen has very sensibly affected the nature of the molecule. Monochloroacetic acid is a much stronger acid than acetic. If β monochloropropionic acid be compared with propionic acid it will be noticed that the difference in properties is much less marked. Since the nature of the sub-

stituting atom is the same in both cases there must be another factor to consider. van't Hoff, ~~considered~~ the influence of one atom upon another in the molecule to be made up of two factors. The first of these is a direct or spacial influence, while the second is an indirect or chain influence, i.e. an influence acting thru the intermediate atoms. Thus, the chlorine in the above named acids exerts a direct influence on the hydroxyl group due to its nearness in the molecule. It also modifies the properties of the carbon atom to which it is bound. This in turn acts on the carboxyl carbon, and the latter on the hydroxyl group. The relative magnitude of these two effects has not been determined.

Michael's Scale of Influence. Following out this idea of van't Hoff, Michael, has developed the following rule for paraffine compounds with a normal carbon chain: The influence of one atom on the others in the molecule is expressed by the scale

1-2-3-5-6-4-7-(9-10-11)-8.

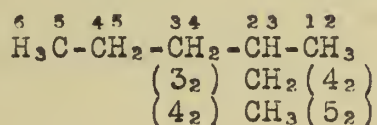
It may make the matter clearer to quote Michael himself on this point: "Um diesen Gegenstand weiter zu verfolgen, ist es nötig, eine Reihenfolge aufzustellen, welche den Gesamteinfluss, daher die Summe der mittelbaren und unmittelbaren Einflüsse, von den Atomen einer normalen organischen Verbindung darstellt, und die folgende Skala entspricht unseren jetzigen Kenntnissen am besten:

1-2-3-5-6-4-7-9-10-11-8.

"Diese Verhältnisse beziehen sich auf Atome, die um zwei an einander gebundene Kolenstoffatome gruppiert sind, und durch 1-2 werden direkt verbundene Atome bezeichnet. Die relativen Stellungen von 9, 10, und 11 unter einander sind unsicher; überhaupt kann nicht nachdrücklich genug hervorgehoben werden, das diese

Zusammenstellung nur provisorisch ist, und die weitere experimentelle Bearbeitung des Gebietes eine grössere Complicirung dieser Verhältnisse zur folgen haben kann. Man kann schon jetzt, wie später entwickelt wird, mit Bestimmtheit annehmen, dass die räumlichen Lagen von Seitenketten verschieden von denen der normalen Kette sind, und nicht mit den Voraussetzungen der van't Hoff'schen Hypothese übereinstimmen.

"Die angewandte Numerirung der Atome folgt, so weit wie möglich, der Genfer Nomenclatur, und die Stellungen der Atome in einer Kette werden auf ¹C bezogen. Bei den Seitenketten bedeutet der Index zu einer Zahl die Eintrittsstelle derselben in die Hauptkette. Es werden z.B. die Atome des Aethyl-2-pentans auf folgende Weise beziffert:



"Von diesem Standpunkte aus wollen wir die Frage von der Positivität des Methyls, sowie die nie bestrittene Annahme, dass dieses Verhältniss in allen Fällen gültig ist, erörtern.

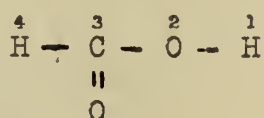
Geht man von CH₄ aus und ersetzt man eines der Wasserstoffatome durch C, so muss im ²C-¹CH₃ das ¹C bedeutend negativer als vorher sein; bringt man zu ²C 3 Wasserstoffatome, so hat der Versuch uns gelehrt, dass ¹C nun positiver ist als in CH₄. Offenbar kann dies nur daher kommen, dass der Gesamteinfluss von ³H grösser, als der von ²C ist.

"Während die Stellungen 2 und 3 von der allergrössten Bedeutung sind, findet man, dass 4 untergeordneter ist, und zwar spielt sie eine geringere Rolle als 5 oder 6. Der Grund dieser Verhältnisse ist darin zu suchen, dass der mittelbare Einfluss von 4 geringer als

3 ist, und ungleich weniger bedeutet als 2; bei der Stellung 4 spielt sogar der mittelbare Einfluss eine so untergeordnete Rolle, dass man für die meisten Fälle 4-5-6-7 als gleichbedeutend annehmen darf. Offenbar handelt es sich von der Stellung 4 an weit mehr um die unmittelbare, räumliche Entfernung der Atome, und daher kommt es, dass 5 und 6 einen bedeutendern Gesamteinfluss als 4 auf 1 ausüben.

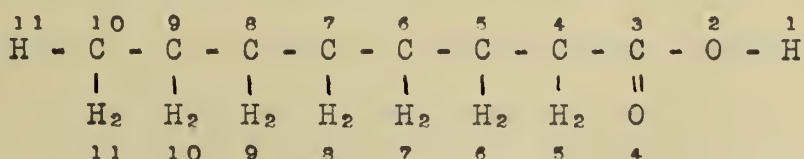
"Nach dieser Auseinandersetzung ist es wohl klar, dass die geläufige Annahme, es sei Methyl stets positiver als Wasserstoff keineswegs selbstverständlich ist. Der Fall kann vorkommen, dass der negativ Kohlenstoff des Methyls einen geringen mittelbaren, aber einen relativ grössern unmittelbaren Einfluss zeigt, nach den beiden Richtungen aufweisen, weshalb ein solches Methyl als negativ auftreten kann. Dass dies wirklich vorkommt, ist am besten an Beispielen zu zeigen.

"Die bedeutungsvollen Untersuchungen von Ostwald über die Affinitätsgrössen organischer Säuren bieten besonders gute Anhaltspunkte zur Ermittlung der Gesamteinflüsse, denn die angewandten Methoden erlauben eine Feinheit und Genauigkeit der experimentellen Resultate, welche in keinen andern Fall wieder vorkommt. Die Acidität einer Säure ist der Ausdruck der relativen Negativität seiner durch Metalle ersetzbaren Wasserstoffatome, und wenn obige Reihenfolge die richtigen Verhältnisse repräsentirt, so müssen die bei ihrer Anwendung deducirten Schlüsse mit den zum Theil noch unverstandlichen Versuchsergebnissen von Ostwald im Einklang sein. Der Austausch von H im



durch CH_3 muss eine sehr bedeutende Verminderung der Acidität zur Folge haben, den Kohlenstoffatome kommt in die untergeordnete Stellung 4, dagegen drei Wasserstoffatome in die bedeutungsvolle Stellung 5, und es fällt K etwa 12 Mal beim Übergang von Ameisen- zu Essigsäure. Ein solcher Sprung in der Constante kann bei der eibasischen, gesättigten Fettsäuren nicht wieder vorkommen, den bei der Bildung der nächsten Homologen handelt es sich um den Ersatz von einem H durch den negativen C, indem beide Atome sich in der wichtigen fünften Stelle befinden, und drei neuen Wasserstoffatome kommen in die sechste, daher an einen minder einflussreichen Platz; hingegen kommt beim Übergang von Ameisensäuren zu Essigsäure der Kohlenstoff in die relativ unwichtigere vierte Stelle, während auf einmal drei wichtige H eingeführt werden. Die Einführung von CH_3 Stelle von H bringt den negativen C an Stelle von H, gleichzeitig H_3 an den wichtigen Platz 6; offenbar wird der Einfluss von H_3 bedeutend durch C vermindert, und der Übergang zur Propionsäure findet deshalb mit einer Verminderung von nur zwei Drittel statt."

Altho Michael has taken a step in the right direction, his rule leaves much to be desired. Consider, for example, the monobasic fatty acids, using his method of numbering the atoms:



An inspection of the ionization constants of the normal acids will show that, beginning with acetic acid, the homologs exhibit very little change when normal alkyl groups are substituted for hydrogen.

	K (25°)
Acetic acid	1.850×10^{-5}
Methyl acetic acid	1.414×10^{-5}
Ethylacetic acid	1.600×10^{-5}
Propylacetic acid	1.700×10^{-5}
Butylacetic acid	1.44×10^{-5}

In this study, Michael's scale can be considered from position 5 outward, thus:

5 - 6 - 4 - 7 - 9 - 10 - 11.

The substitution of a negative group in position 5 will have a very marked effect on the ionization constant of the acid, as is shown in the case of acetic- and chloroacetic acids:

	K(25°)
Acetic acid	1.850×10^{-5}
Chloroacetic acid	1.55×10^{-3}

In harmony with the theory, chlorine in position 6 will be far less influential. This is shown by the ionization constants of propionic- and the chloropropionic acids.

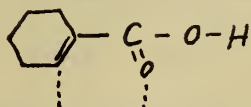
Propionic acid	1.414×10^{-5}	
α Chloropropionic acid	1.47×10^{-3}	(5)
β Chloropropionic acid	$8/59 \times 10^{-5}$	(6)

Next, Michael follows positions 5 and 6 by 4. That is to say, a substituent in the latter position will modify the properties of the acid to a lesser degree than it would in the either of the former. Then a substituted formic acid should differ but little from formic acid itself. Unfortunately negatively substituted acids such as chloroformic- and bromoformic acids do not exist under conditions in which they may be studied. Altho Michael did not extend his rule so as to include negative groups as well as atoms, it is interesting to consider the the effect of the substitution of the phenyl radical. One might look upon benzoic acid as phenylformic acid. Here the negative phenyl has been substituted for the positive hydrogen. A comparison of the ionization constants of the acids shows a decrease rather than an increase in the acid strength, altho the numerical difference in the constants is in agreement with the theory.

Formic acid
Benzoic acid

$K(25^{\circ})$
 2.14×10^{-4}
 6.69×10^{-5}

The effect of the phenyl radical in this position is opposite to its effect in any other position in the carbon chain. This unusual behavior might be expected in the light of Thiele's studies. Here the carbonyl oxygen is conjugated with the phenyl thus:



It seems then, that the place of 4 in the scale is based upon rather meager data. Again, positions 9 - 10 - 11 are given preference to 8. It is difficult to see the reason for this since the available data is so limited and inaccurate.

The Ostwald Factor. Reference has already been made to Ostwald's correlation of ionization and structure. Ostwald, has indicated that in certain positions in the molecule the dissociation constants are changed by a more or less constant factor. If we designate by k_1, k_2, k_3 etc. the ionization constants of the acids in which a certain group or atom occupies the same relative position to the carboxyl; and, by $k_1', k_2', k_3',$ etc. the constants of the corresponding unsubstituted acids; it follows that $\frac{k_1}{k_1'} = \frac{k_2}{k_2'} = \frac{k_3}{k_3'},$ etc. will be constant. This is known as the Ostwald Factor Law. It is not of universal validity since two substituents mutually affect each other. Also the factor depends upon the constitution of the acid as well as the nature of the substituent. It takes different values for aliphatic and for aromatic compounds. Furthermore, numerical values for the factor may be determined for compounds of analogous constitution, only. A discussion of the choice of the ionization constant, rather than its logarithm, will be taken up later.

Wegscheider's Development of the Ostwald Rule. Wegscheider₄

took up the study of the influence of substitution on the affinity constants of organic acids, and calculated certain factors, by means of Ostwald's Law, for various substituents in given positions. Thus, the factor for chlorine in the α and β positions in 90 and 6.2 respectively. The ionization constant of the unsubstituted acid multiplied by the factor for the substituent will give the constant for the substituted acid thus,

		K calc.	K measured
Chloroacetic acid	$1.850 \times 10^{-4} \times 90 =$	1.66×10^{-3}	(1.55×10^{-3})
α Chloropropionic acid	$1.414 \times 10^{-5} \times 90 =$	1.27×10^{-3}	(1.47×10^{-3})
α Chlorobutyric acid	$1.66 \times 10^{-5} \times 90 =$	1.44×10^{-3}	(1.39×10^{-3})
β Chloropropionic acid	$1.414 \times 10^{-5} \times 6.2 =$	8.76×10^{-5}	(8.59×10^{-5})
β Chlorobutyric acid	$1.60 \times 10^{-5} \times 6.2 =$	9.92×10^{-5}	(9.94×10^{-5})

The following Table taken from Wegscheider's paper contains in the first column the substituents studied. In the other columns are found the various factors for the positions indicated at the top of each;

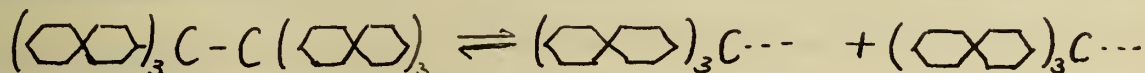
Table I.

Radical.	Position of the Substituent in the Chain.							
	α	β	γ	δ	ϵ	ζ	η	ν
Cl	90	6.2	2.0	1.27	?	-	-	-
Br	76	7.3	1.76	1.19	-	-	-	-
I	42	6.72	1.53	1.66	-	-	-	-
F	-	-	-	-	-	-	-	-
CN	20.5	-	-	-	-	-	-	-
NO ₂	-	12.5	-	-	-	-	-	-
OH	8.4	2.31	-	-	-	-	-	-
OCH ₃	18.6	-	-	-	-	-	-	-
OC ₂ H ₅	13	?	-	-	-	-	-	-
SH	12.5	-	-	-	-	-	-	-
CH ₃	0.74	1/12	1.0	0.90	0.90?	1.10?	0.78?	-
	1.10							
C ₂ H ₅	0.83	1.20	0.98	0.81	0.99	0.85	-	-
	1.31							
C ₆ H ₅	3.1	1.7	-	-	-	-	-	-
SO ₃ CH ₃	-	-	-	-	-	-	-	-
COOH	34	2.41	1.67	1.2	1.2	1.2	-	1.2
COOCH ₃	-	2.4	-	-	-	-	-	-
COOC ₂ H ₅	27	2.25	-	1.53?	-	1.11	-	1.28

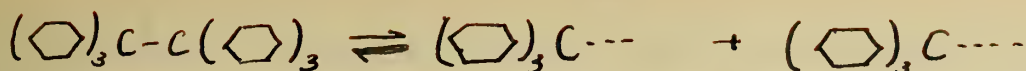
The table plainly indicates that the influence of negative groups or atoms in the α position is much more pronounced than in any other position. It can furthermore be seen that the factors for the methyl and ethyl groups have values close to unity in all positions. This bears out the statement made earlier in the paper that the influence of the normal hydrocarbon radical may usually be neglected. Again the table emphasises the meagerness of the data.

Wegscheider further studied the aromatic acids - particularly the derivatives of benzoic acid. Here he found that the factor for the ortho position was much larger numerically than that for the meta or para positions. However, the difference between the ortho and meta or para factors was found to be smaller than the difference between the α and β positions in the aliphatic series.

The Flurscheim Factors. Flurscheim attributes the effect of negative substitution to three factors. These are, 1) the polarity of the substituent, 2) the amount of affinity taken up by the substituent, and 3) steric hindrance. He develops the suggestion of Werner that different substituents on the carbon atom take up different amounts of affinity from the latter; the saturation capacity of the carbon being constant. Thus, in hexadiphenylethane the three diphenyl groups take up so much of the affinity of the carbon atom that the molecule easily disrupts yielding two molecules of tridiphenylmethyl,



In hexaphenylethane the lighter phenyl groups take up less of the affinity of the carbon atoms than the diphenyl groups would, consequently, the equilibrium is displaced to a lesser degree to the right than it is in the case of hexadiphenylethane,



Flurscheim illustrates his point somewhat as follows: In α anilinopropionic acid we have a compound that is a stronger acid than propionic acid. The negativ group takes up more of the available energy of the α carbon atom than does the hydrogen which has been displaced. This leads to a reduction of the affinity between the α carbon atom and the carboxyl carbon, followed by an increase in the affinity between carboxyl carbon an oxygen, with a consequent decrease between oxygen and hydrogen. It is tacitly assumed that decrease in affinity between oxygen and hydrogen results in an increase in the magnitude of the ionization constant.

On the other hand, β anilinopropionic acid is a weaker acid than propionic. In this case the negative group taking up a large portðon of the affinity of the β carbon atom causes the affinity of this for the α carbon to decrease. This results in a strengthening of the bond between α carbon and carboxyl carbon, followed by a weakening of the attraction of the latter for oxygen. Finally the oxygen can be bound to the hydrogen by a stronger tie. The following formulae illustrate the case graphically. The thick lines indicate the bonds strengthened by the presence of the negative group.

Propionic acid,		K 1.414×10^{-6}
α Anilinopropionic acid,	$\text{C}_6\text{H}_5\text{NH}-\overset{\text{CH}_3}{\underset{ }{\text{CH}}}-\text{C}\overset{\text{O}}{\parallel}-\text{O}-\text{H}$	2.2×10^{-5}
β Anilinopropionic acid,	$\text{C}_6\text{H}_5\text{NH}-\text{CH}_2-\text{CH}_2-\text{C}\overset{\text{O}}{\parallel}-\text{O}-\text{H}$	0.4×10^{-5}

The theory is also applied to ortho-, meta-, and para-chlorobenzoic acids, and to the corresponding bromobenzoic acids. It was not, however, applied to the halogen substituted fatty acids. According to the theory, the α, β, γ and δ halo-paraffin acids should

be alternately stronger and weaker than the corresponding unsubstituted acids. An inspection of the ionization constants shows that this is not the case.

	Ka		Ka
Butyric acid	1.6×10^{-5}	α Chlorobutyric acid	1.39×10^{-3}
		β Chlorobutyric acid	8.94×10^{-6}
Valerianic acid	1.7×10^{-5}	γ Chlorobutyric acid	3.00×10^{-6}
		δ Chlorovalerianic acid	2.04×10^{-5}

Flurscheim did not study the effect of negative substitution beyond the β position. Further, his choice of the anilino-acids was unfortunate because here one has to deal with a decidedly amphoteric substance.

Derick's Measure of Combined Direct and Indirect Influences.

From thermodynamic considerations, Derick, has decided to use a free energy function - the logarithm of the ionization constant - as a measure of the tendency of a reaction to occur. This is justified by an inspection of the equation

$$A = RT \ln K,$$

in which A is the free energy of ionization, R is the gas constant, and T is the absolute temperature.

As a measure of polarity Derick uses $\frac{-1000}{\ln K}$. It will be noticed that the logarithm of the ionization constants for most organic acids and bases are negative in sign. This means that work must be done on the compound to bring about complete ionization. The more negative the group the less the work necessary. By taking $\frac{-1000}{\ln K}$ a convenient standard is obtained. The following table, which is a part of that given in Derick's paper illustrates the point. θ and ϕ stand for the negative and positive polarity of the group. That is; $\theta = \frac{-1000}{\ln K}$.

		Ka	log K	θ	ϕ
Phenyl	C ₆ H ₅ -	1.3 $\times 10^{-10}$	-9.886	101.5	
α -Chlorobutyryl	C ₂ H ₅ CHClCO-	1.39 $\times 10^{-3}$	-2.857	350.0	
Acetyl	CH ₃ CO-	1.86 $\times 10^{-4}$	-4.731	211.0	
Benzoyl	C ₆ H ₅ CO-	6.9 $\times 10^{-5}$	-4.161	240.0	
Kb					
Ammonium	NH ₄ -	1.87 $\times 10^{-6}$	-4.728		211.4
Methylammonium	CH ₃ NH ₃ -	5.0 $\times 10^{-7}$	-3.301		202.8

Having defined polarity Derick then passes to a study of the effect of substitution of negative and positive groups and atoms on the molecule. He says, " Since each atom in the molecule exerts a direct and an indirect influence upon the ionization, the ionization constant for a given ionizing group expresses the resultant of the combined influence of the direct and indirect factors of every atom in the molecule. Table II will show that the combined influence of hydrogen or an alkyl radical is very small, and their substitution into a given molecule has little effect upon the ionization and therefore their combined influence (direct and indirect) is very small..... In the case of the other atoms the combined direct and indirect influences may be very great.... To determine the influences of the direct and indirect factors for a given radical, we must substitute it into a given acid and note the effect in the change of the ionization constant. Since the ionization constant of the unsubstituted acid expresses the combined influences of all the atoms in the molecule, the change in the ionization constant produced by substituting a given group for hydrogen will express the value of the combined direct and indirect influences of the substituent. By varying the position of the substituent with reference to the ionizing group the combined direct and indirect influences of the substituent with reference to the ionizing group may be determined. A correction for hydrogen displaced should be applied, but

since it is so small it may be safely neglected without appreciably changing the relative results desired.

"The method of application of this measure of the scale of combined influence of the direct and indirect influence of substituents will be illustrated by the following: Suppose it is desired to test the relative scale of combined influence for chlorine when substituted in different positions of a normal fatty acid, say, butyric acid....First determine the ratio of the combined direct and indirect influence of the atom in the substituted and unsubstituted acids, thus α chlorobutyric acid : butyric acid = $-1000/\ln K(\alpha\text{chlorobutyric})$: $-1000/\ln K(\text{butyric}) = \log K(\text{butyric}) / \log K(\alpha\text{chlorobutyric}) = -4.807 / -2.857 = 1.682 / 1$.

$$\beta\text{Chlorobutyric} : \text{butyric} = (-4.807) : (-4.049) = 1.186 : 1$$

$$\gamma\text{Chlorobutyric} : \text{butyric} = (-4.807) : (-4.523) = 1.062 : 1$$

$$\delta\text{Chlorovalerianic} : \text{valerianic} = (-4.796) : (-4.690) = 1.022 : 1$$

Subtracting the combined influence of the other atoms in the molecule (which is equal to the logarithm of the ionization constant of butyric acid and approximately equal to one in the above ratio, neglecting the effect of the displaced hydrogen) we have:

$$\alpha\text{factor} = 1.682 - 1 = 0.682$$

$$\beta\text{factor} = 1.186 - 1 = 0.187$$

$$\gamma\text{factor} = 1.062 - 1 = 0.062$$

$$\delta\text{factor} = 1.022 - 1 = 0.022$$

Therefore the relative scale of the combined direct and indirect actions of chlorine in the α , β , γ and δ positions as measured by the carboxyl group in the α position is:

$$\alpha : \beta : \gamma : \delta = 0.682 : 0.186 : 0.062 : 0.022 "$$

From this it can be seen that the effect of substitution

for negative groups decreases as the substituent is moved out the chain.

If we call the α factor 1 we have the approximate ratios

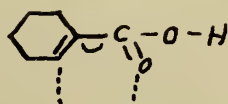
$$\alpha : \beta : \gamma : \delta = 1 : \frac{1}{3} : \frac{1}{9} : \frac{1}{27}.$$

This is known as Derick's 'Rule of Thirds'. It holds not only for the acids mentioned above, but for most negatively substituted acids. By means of this rule the structure of substituted acids can be determined if the ionization constants of the substituted and unsubstituted acids are known and if the α place factor has been determined for the substituent in question. Conversely, the ionization constant of a negatively substituted acid can be calculated from the α place factor for the substituting group and the ionization constant of the unsubstituted acid.

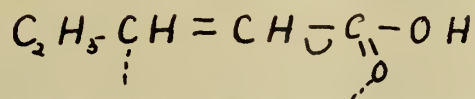
Flurscheim ⁷ looked upon the unsaturated linkage as a negative group. This offers a notable exception to the general rule that the effect diminishes from α carbon outward. Consider, for example, the ionization constants of the olefinic acids.

		Ka
Δ^1 Pentenic acid	$C_2H_5CH=CHCOOH$	1.48×10^{-5}
Δ^2 Pentenic acid	$CH_3CH=CHCH_2COOH$	3.35×10^{-5}
Δ^3 Pentenic acid	$CH_2=CH(CH_2)_2COOH$	2.09×10^{-6}
Δ^1 Hexenic acid	$C_3H_7CH=CHCOOH$	1.89×10^{-5}
Δ^2 Hexenic acid	$C_2H_5CH=CHCH_2COOH$	2.64×10^{-5}
Δ^3 Hexenic acid	$CH_3CH=CH(CH_2)_2COOH$	1.74×10^{-6}
Δ^4 Hexenic acid	$CH_2=CH(CH_2)_3COOH$	1.91×10^{-5}

It will be remembered that, in the case of formic and benzoic acids, the substitution of the negative phenyl for positive hydrogen reduced the value of the ionization constant instead of increasing it as the theory would demand. It was pointed out that this anomalous behavior might be attributed to the conjugated double linkage.



Here, again, in the Δ ,Pentenic- and Δ ,Hexenic acids appears a double linkage conjugated with the carbonyl oxygen.



It seems that in some way when the double linkage is thus conjugated with the carbonyl oxygen, its negative nature is diminished. (When the term 'double linkage' is used ,it is not intended to imply that the atoms are linked together by more than one bond, as the structural formula would indicate; but that, there appears that peculiar type of unsaturation characteristic of the olefinic hydrocarbons.)

While the effect of negative substitution on the α carbon atom is very marked, as has been pointed out; the effect diminishes very rapidly on the β , γ and δ carbon atoms. If any generalities are to be proposed for positions further out on the chain, it is obvious that the ionization constants must be measured with a very much greater degree of accuracy than they have been heretofore. When reference is made to the literature, one is astonished at the divergence of results obtained by various investigators. The constants used for purposes of illustration up to this time have, for the most part, been taken from H. Lunden's "Affinitätsmessungen an Schwachen Säuren und Basen". In the succeeding sections of this thesis, the methods of detecting errors in conductivity data, and the preparation and measurement of pure materials, will be taken up in detail; with a view toward obtaining a more accurate insight into the laws governing the reciprocal influence of the various atoms in the molecule.

III THEORETICAL.

Calculated Λ_0 as a Criterion of Precision and of Constant Errors. It can be shown that constant values for the ionization constant of an acid may be found for several dilutions, and yet these values may not be near the true one. This is due, in part, to constant errors in measurement, and in part, to small amounts of impurities in the material taken for measurement. Analysis of the substance may fail to show traces of foreign matter, which may yet be present in sufficient amount to affect the value of the ionization constant. Derick and Brady have observed that pyrrolacemic acid, for example, may be contaminated with as much as forty per cent of acetic acid before ultimate analysis will show the presence of this impurity.

To detect constant errors in measurement, and to discover small amounts of contaminating substances, Derick, has proposed the use of calculated Λ_0 - the conductivity at infinite dilution. This criterion can be used only for dilute solutions of weak electrolytes, where the ideal mass law

$$k = \frac{C \alpha^2}{1 - \alpha}$$

may be assumed to hold. Since $\alpha = \frac{\Lambda}{\Lambda_0}$, this expression takes the form

$$K = \frac{C \Lambda^2}{\Lambda_0 (\Lambda_0 - \Lambda)}$$

Λ_0 can be calculated from the above equation, using any two dilutions C and C_1 .

$$\frac{C \Lambda^2}{\Lambda_0 (\Lambda_0 - \Lambda)} = \frac{C_1 \Lambda_1^2}{\Lambda_0 (\Lambda_0 - \Lambda_1)}$$

$$\therefore \Lambda_0 = \frac{\Lambda \Lambda_1 (C \Lambda - C_1 \Lambda_1)}{C \Lambda^2 - C_1 \Lambda_1^2}$$

This calculated Λ_0 should be a constant and should have a value equal to that found by the 'Salt method' if the conductance data is accurate and no impurities are present.

The salt method is based on Kohlrausch's principle that the molar conductance at zero concentration is made up additively of the conductance of the ions present.

$$1. \Lambda_{0RCOOH} = \Lambda_{0RCOO^-} + \Lambda_{0H^+}$$

$$2. \Lambda_{0RCOONa} = \Lambda_{0RCOO^-} + \Lambda_{0Na^+} \text{ or } \Lambda_{0RCOO^-} = \Lambda_{0RCOONa} - \Lambda_{0Na^+}$$

Substituting this last value in the first equation, we obtain

$$3. \Lambda_{0RCOOH} = \Lambda_{0RCOONa} - \Lambda_{0Na^+} + \Lambda_{0H^+}$$

It is not necessary to have the most accurate conductivity data for the sodium salt of the acid because the molar conductivity of most salts of weak electrolytes falls between 80 and 90, the mobility of the sodium ion at 25° being 52. But the mobility of the hydrogen ion, being such a large number, should be known with a much greater degree of accuracy. Unfortunately the values for this ion have been given values from 338 to 365. The best value seems to be that of Kendall, and is 347.2. This value will be used in the calculations of this paper.

In the article previously mentioned Derick has carefully considered the effect of errors in Λ and Λ_0 , upon the ionization constant, and upon the calculated Λ_0 . Assuming the errors in the concentration, C , to be negligible, the percentage error in k due to errors in Λ and Λ_0 is obtained by differentiating the logarithmic form of the expression

$$K = \frac{C\Lambda^2}{\Lambda_0(\Lambda_0 - \Lambda)}$$

$$\frac{dK}{K} = \left(\frac{2\Lambda_0 - \Lambda}{\Lambda_0 - \Lambda} \right) \left(\frac{d\Lambda}{\Lambda} - \frac{d\Lambda_0}{\Lambda_0} \right)$$

As the concentration increases Λ approaches 0 and the expression becomes

$$\frac{dK}{K} = 2 \left(\frac{d\Lambda}{\Lambda} - \frac{d\Lambda_0}{\Lambda_0} \right)$$

As the solution becomes more and more dilute Λ approaches Λ_0 , when we have

$$\frac{dK}{K} = \infty \left(\frac{d\Lambda}{\Lambda} - \frac{d\Lambda_0}{\Lambda_0} \right)$$

Thus the accuracy with which k can be determined will increase with increasing concentration as long as the mass law holds. For most weak electrolytes this upper limit has been found to be in the neighborhood of 0.02 Normal.

In order to determine which values of calculated Λ_0 are the most sensitive to errors in Λ and Λ_1 , the logarithmic form of the equation

$$\Lambda_0 = \frac{\Lambda \Lambda_1 (C \Lambda - C_1 \Lambda_1)}{C \Lambda^2 - C_1 \Lambda_1^2}$$

is differentiated.

$$\frac{d\Lambda_0}{\Lambda_0} = \frac{C_1 \Lambda_1 (C \Lambda_1^2 + C \Lambda^2 - 2 C \Lambda \Lambda_1) d\Lambda}{(C \Lambda - C_1 \Lambda_1) (C \Lambda^2 - C_1 \Lambda_1^2) \Lambda} + \frac{C \Lambda (C_1 \Lambda_1^2 + C \Lambda^2 - 2 C_1 \Lambda \Lambda_1) d\Lambda_1}{(C \Lambda - C_1 \Lambda_1) (C \Lambda^2 - C_1 \Lambda_1^2) \Lambda_1}$$

The errors in C and C_1 are again assumed to be negligible. Table III contains Kendalls measurements on acetic acid with Derick's calculations of Λ_0 . In this and the following tables

C (v)	stands for	concentration
\underline{L}^c	" "	Specific conductivity corrected for water
\underline{L}^u	" "	" " uncorrected " "
\underline{L}_{H_2O}	" "	" " of the water
k_a^c	" "	Ionization constant corrected for water
k_a^u	" "	" " uncorrected " "
Λ^c	" "	Molar conductivity corrected for water
Λ^u	" "	" " uncorrected " "
$\Lambda_0^c (\Lambda_0^u)$	" "	Molar conductivity at zero concentration corrected and uncorrected for water.

$$\text{Let } a = \frac{C, \Lambda, (C, \Lambda_1^2 + C \Lambda^2 - 2 C, \Lambda \Lambda_1)}{(C \Lambda - C, \Lambda_1)(C \Lambda^2 - C, \Lambda_1^2)} \quad \text{and}$$

$$b = \frac{C \Lambda (C, \Lambda_1^2 + C \Lambda^2 - 2 C, \Lambda \Lambda_1)}{(C \Lambda - C, \Lambda_1)(C \Lambda^2 - C, \Lambda_1^2)}$$

Using the data given in Table III the following values are obtained:

Table II 10

C	C ₁	k	k ₁	a	b
1/54.28	1/108.56	1.849 × 10 ⁻⁵	1.849 × 10 ⁻⁵	-110.5	+111.2
1/54.28	1/434.2	1.849 × 10 ⁻⁵	1.849 × 10 ⁻⁵	- 33.4	+ 34.4
1/54.28	1/6948	1.849 × 10 ⁻⁵	1.870 × 10 ⁻⁵	- 5.3	+ 6.3
1/108.56	1/217.1	1.849 × 10 ⁻⁵	1.851 × 10 ⁻⁵	-151.1?	+151.1?
1/217.1	1/434.2	1.851 × 10 ⁻⁵	1.849 × 10 ⁻⁵	- 71.5	+ 72.5
1/434.2	1/868.4	1.849 × 10 ⁻⁵	1.850 × 10 ⁻⁵	- 51.6	+ 52.7
1/868.4	1/1737	1.850 × 10 ⁻⁵	1.854 × 10 ⁻⁵	- 36.0	+ 37.3

The error in calculated Λ_0 for acetic acid is never greater than that in Λ or Λ_1 , as long as $\frac{d\Lambda}{\Lambda}$ and $\frac{d\Lambda_1}{\Lambda_1}$ have the same sign since a and b are opposite in sign. As long as this is true Λ_0 may be found with the same accuracy with any combinations of Λ and Λ_1 . If $\frac{d\Lambda}{\Lambda}$ and $\frac{d\Lambda_1}{\Lambda_1}$ are opposite in sign the error is greater with greater values of concentration.

Applying the criterion of calculated Λ_0 to Kendall's measurements on acetic acid (see Table III) it is evident that his data is accurate. Likewise, Prasil's data on Phenylacetic acid (Table IV) shows the necessary precision. In order to show the effect of minute traces of impurities on the ionization constants and on calculated Λ_0 the data for the measurement of two samples of β phenylpropionic acid are given in Tables V and VI. The first of these acids was recrystallized several times from low boiling petroleum ether until a constant melting point was obtained. The second sample was synthesized with particular care and was finally purified by distillation under diminished pressure. The purified product was again distilled under diminished pressure and preserved in a desiccator. Water with a specific conductivity less than 0.8×10^{-6} was used in making up the solutions for both acids.

Table III.

Conductivity Data for Acetic Acid. (Kendall) //

v	$L \times 10^4$	$L \times 10^4$	$L_{H_2O} \times 10$	$k \times 10^5$	$k \times 10^5$
13.57	4.476	4.485	0.204	1.845	1.839
27.14	3.156	3.165	0.284	1.851	1.839
45.28	2.218	2.227	0.404	1.849	1.833
108.36	1.555	1.564	0.575	1.849	1.826
217.1	1.088	1.097	0.820	1.851	1.821
434.2	0.7561	0.7651	1.17	1.849	1.804
868.4	0.5222	0.5312	1.69	1.850	1.784
11737.0	0.3571	0.3661	2.46	1.854	1.754
3474.0	0.2406	0.2496	3.60	1.855	1.706
6948.0	0.1592	0.1682	5.35	1.870	1.639

Dilution series.	Λ^o	Λ^c	Dilution series.	Λ^o	Λ^c
13.57 and 27.14	766	443.0	868.4 and 1737.0	400	303.3
45.28	449	341.1	3474.0	381	299.2
108.36	359	319.6	6948.0	401	299.9
217.1	416	326.7	1737.0 " 3474.0	390	296.7
434.2	402	313.8	6948.0	401	299.0
868.4	399	325.4	3474.0 " 6948.0	409	300.4
1737.0	399	308.0			
3474.0	396	304.0			
6948.0	400	302.8			
27.14 " 54.28	348	294.0	Λ^o by the salt method	387.7	
108.56	311	296.0			
217.1	389	314.1			
434.2	384	305.5			
868.4	388	313.4			
1737.0	532	304.6			
3474.0	391	301.7			
6948.0	458	301.3			
54.28 and 108.56	290	297.3			
217.1	402	320.4			
434.2	391	306.7			
868.4	392	306.4			
1737.0	395	305.2			
3474.0	393	301.9			
6948.0	399	301.5			
108.56 " 217.1	551	338.6			
434.2	434	303.2			
868.4	414	307.8			
1737.0	408	306.0			
3474.0	401	302.3			
6948.0	403	301.7			
217.1 " 434.2	379	293.6			
868.4	388	300.3			
1737.0	393	301.7			
3474.0	392	299.4			
6948.0	398	300.0			
434.2 " 868.4	394	304.8			
1737.0	398	304.0			
3474.0	394	300.4			
6948.0	400	300.5			

Table IV.

Conductivity Data for Phenylacetic Acid. (Prasil),₂

Concentrations.	Λ^u	Λ^c
0.01	26.35	26.29
0.0075	30.27	30.14
0.0050	36.73	36.54
0.0025	50.86	50.47
0.0010	77.25	77.16
0.00075	87.04	86.92
0.00050	104.10	102.19
0.00025	137.54	133.74
0.00010	191.02	181.52

Dilution series.		Λ^u	Λ^c	
0.01	and	0.0075	389.8	389.6
		0.0050	377.3	328.8
		0.0025	376.1	334.6
		0.0010	385.6	393.1
		0.00075	358.6	362.8
		0.00050	378.4	336.7
		0.00025	374.7	330.6
		0.00010	372.9	322.9
0.0075	"	0.0050	378.5	341.3
		0.0025	376.3	339.5
		0.0010	386.3	400.9
		0.00075	357.7	366.4
		0.00050	378.5	337.9
		0.00025	274.1	331.2
		0.00010	372.9	323.1
0.0050	"	0.0025	375.3	338.7
		0.0010	387.4	411.0
		0.00075	355.6	369.3
		0.00050	378.6	337.7
		0.00025	373.3	330.8
		0.00010	373.0	322.7
0.0025	"	0.0010	393.5	458.6
		0.00075	349.7	380.6
		0.00050	379.3	337.5
		0.00025	373.7	329.9
		0.00010	372.6	322.0
0.0010	"	0.00075	355.4	279.9
		0.00050	368.4	280.9
		0.00025	367.8	304.9
		0.00010	370.1	310.9
0.00075	"	0.00050	452.5	281.5
		0.00025	338.1	309.0
		0.00010	377.6	313.0
0.00050	"	0.00025	367.4	321.8
		0.00010	370.4	317.1
0.00025	"	0.00010	371.6	315.2

 $k_a^u \times 10^5$

5.171

5.171

5.171

5.171

5.188

5.103

5.169

5.167

5.081

Table V.

Conductivity Data for β Phenylpropionic Acid. (Impure)

C	Λ^0	$k_a^0 \times 10^5$
0.01N	17.477	2.265
0.0075	20.114	2.266
0.0050	24.480	2.266
0.0025	34.187	2.272
0.0010	52.264	2.243
0.00055	59.242	2.203
0.00050	71.057	2.201
0.00025	95.535	2.162
0.00010	137.150	2.094

Dilution series.		Λ^0
0.01	and 0.0075	417.6
	0.0050	385.6
	0.0025	403.1
	0.0010	346.6
	0.00075	329.5
	0.00050	326.4
	0.00025	326.0
	0.00010	328.8
0.0075	" 0.0050	368.9
	0.0025	403.1
	0.0010	342.0
	0.00075	315.4
	0.00050	330.9
	0.00025	330.0
	0.00010	375.7
0.0050	" 0.0025	416.3
	0.0010	339.0
	0.00075	310.6
	0.00050	321.2
	0.00025	322.5
	0.00010	327.0
0.0025	" 0.0010	311.5
	0.00075	286.8
	0.00050	305.2
	0.00025	314.1
	0.00010	323.2
0.0010	" 0.00075	243.9
	0.00050	304.5
	0.00025	315.0
	0.00010	324.8
0.00075	" 0.00050	365.9
	0.00025	332.0
	0.00010	332.2
0.00050	" 0.00025	319.0
	0.00010	326.6
0.00025	" 0.00010	332.2

Table VI.

Conductivity Data for β -Phenylpropionic Acid. (Pure)

C	$L_{H_2O} \times 10^6$	Λ^u	Λ^c	$k_{\infty}^u \times 10^5$	$k_{\infty}^c \times 10^5$
0.01N	0.50	17.499	17.450	2.270	2.258
0.0075	0.60	20.125	20.040	2.269	2.249
0.0050	0.66	24.506	24.375	2.270	2.246
0.0025	0.65	34.160	33.900	2.269	2.232
0.0010	0.65	52.534	51.885	2.268	2.208
0.00075	0.65	59.843	58.970	2.253	2.187
0.00052	0.60	71.788	70.580	2.252	2.168
0.00025	0.65	97.000	94.394	2.246	2.103
0.00010	0.65	140.800	134.260	2.239 _{cc}	1.982

Dilution series.

 Λ^u Λ^c

0.01N	and	0.0075	349.7	256.4
		0.0050	380.4	304.5
		0.0025	370.6	308.7
		0.0010	373.1	314.5
		0.00075	362.4	307.1
		0.00050	356.3	309.4
		0.00025	360.4	304.1
		0.00010	364.3	304.4
0.0075	"	0.0050	401.5	342.7
		0.0025	374.5	320.4
		0.0010	370.7	243.6
		0.00075	344.0	310.6
		0.00050	356.4	312.1
		0.00025	360.8	301.7
		0.00010	366.9	311.6
0.0050	"	0.0025	364.0	311.6
		0.0010	371.8	316.8
		0.00075	335.8	307.5
		0.00050	353.1	310.0
		0.00025	359.0	482.0
		0.00010	366.2	210.5
0.0025	"	0.0010	374.5	319.4
		0.00075	318.0	306.2
		0.00050	350.6	309.6
		0.00025	358.5	303.2
		0.00010	266.3	303.3
0.0010	"	0.00075	155.3	280.4
		0.00050	332.4	302.2
		0.00025	353.3	298.4
		0.00010	365.1	303.5
0.00075	"	0.00050	475.7	316.4
		0.00025	420.4	301.7
		0.00010	408.5	257.7
0.00050	"	0.00025	370.3	296.0
		0.00010	373.5	342.4
0.00025	"	0.00010	374.2	303.3

Table VII.

Conductivity Data for Propionic Acid, (Brady)₁₃C $k \times 10^5$

0.02000	1.4160
0.01000	1.4156
0.00750	1.4156
0.00500	1.4153
0.00250	1.4148
0.00100	1.4153
0.00075	1.4150
0.00050	1.4159
0.00025	1.4144
0.00010	1.4144

Ave = 1.4152 \pm .0005C Λ^0 Λ^c C Λ^0 Λ^c

0.0200 and 0.01000	375.00	290.57	0.00250 and 0.00100	382.58	287.27
	0.00750	375.48	290.92		0.00075 383.56 287.74
	0.00500	376.29	314.95		0.00050 383.80 286.46
	0.00250	380.74	291.87		0.00025 384.16 312.80
	0.00100	381.37	289.64		0.00010 384.54 276.76
	0.00075	382.15	289.47	0.0010 and	0.00075 385.76 288.35
	0.00050	382.67	288.12		0.00050 384.96 286.00
	0.00025	383.29	306.69		0.00025 384.68 324.85
	0.00010	384.00	278.42		0.00010 384.71 275.21
0.0100 and 0.00750	376.31	291.00	0.00075 and	0.00050	384.56 285.73
	0.00500	377.18	350.04		0.00025 384.64 333.62
	0.00250	381.85	292.24		0.00010 384.66 274.54
	0.00100	382.20	289.28	0.00050 and	0.00025 384.59 364.26
	0.00075	382.89	316.78		0.00010 384.64 273.40
	0.00050	383.27	287.93	0.00025 and	0.00010 384.63 239.20
	0.00025	383.69	307.86		
	0.00010	384.16	278.10		
0.00750 and 0.00500	377.77	399.38			
	0.00250	382.90	292.34		
	0.00100	382.68	289.26		
	0.00075	383.32	289.22		
	0.00050	383.62	287.77		
	0.00025	383.90	308.50		
	0.00010	384.21	277.91		
0.00500 and 0.00250	385.12	206.27			
	0.00100	384.00	243.52		
	0.00075	383.91	247.89		
	0.00050	384.06	250.77		
	0.00025	384.20	274.80		
	0.00010	384.45	249.40		

A consideration of the data given in Tables V and VI will bring out a number of interesting facts. In the first place it is obvious that the acid corresponding to Table V must contain an impurity which affects both the ionization constant and the calculated Λ_0^v . It will be observed that from the 0.0025N concentration down there is a marked falling off in the value for k , as well as, for calculated Λ_0^v . Again the values for calculated Λ_0^v seldom approach the value determined by the salt method, which is 376.1 reciprocal ohms. This steady drop in the values for K and Λ_0^v clearly indicate the presence of some impurity. Furthermore, there is apparently an error in the measurement of the conductivity of the 0.00075N dilution. On the whole, the values for calculated Λ_0 are consistently low.

Much better results may be found in Table VI. Here the greatest deviations in the values for the ionization constant are not more than thirty-two parts in twenty-two hundred. If the last two dilutions are ignored, the greatest deviation is eighteen parts in twenty-two hundred. One is justified in discarding the last two dilutions because no sharp zero points on the telephone could be obtained at such low concentrations. A better value for calculated Λ_0^v is found here than in Table V. But here again, there seems to be an error in the measurement of the 0.00075N solution, as indicated by calculated Λ_0^v .

It will be noticed that there is the greatest deviation in calculated Λ_0^v for concentrations that fall near each other. In all such cases $(C\Lambda^2 - C_1\Lambda_1^2)$ and $(C\Lambda - C_1\Lambda_1)$ are small numbers and magnify the errors of measurement.

Table VII, containing the data for propionic acid, shows

the most consistent values for Λ° and for the ionization constant. These measurements are, without doubt, the most accurate that have been made upon this acid.

It is interesting to apply the criterion, calculated Λ° , to Ostwald's data on β phenylpropionic acid₁₄. The following table contains his values for the ionization constant, and also the values for Λ° expressed in Siemen's Units:

v	Λ°	100k
64	13.17	0.00226
128	18.49	0.00227
256	25.76	0.00227
512	35.91	0.00230
1024	49.08	0.00228

	352.0	

In order to convert the values for Λ° and Λ° into International Ohms, it is necessary to multiply by 1.063. Table VIII contains Λ° and Λ° expressed in the modern units.

Table VIII.

v	Λ°
64	14.000
128	19.614
256	27.383
512	38.172
1024	52.172

	374.2

Calculated Λ°

Dilutions	Λ°
64 and 128	140.4
256	209.6
512	268.0
1024	257.8
128 and 256	325.3
512	416.7
1024	301.4
256 and 512	408.5
1024	301.4
512 and 1024	250.1

It is evident that the data lacks precision. There is little agreement between the calculated value for Λ_0^v and that obtained by the salt method.

As has been mentioned before, the value for Λ_0^v for β -phenylpropionic acid obtained by the salt method is 376.1. This value can be checked by comparing it with one obtained by a method suggested by Ostwald. According to the rule proposed, ~~for~~ the conductivity at zero concentration is a function of the number of atoms in the molecule, provided that the number of atoms exceeds 12. For all acids having the same number of atoms, the conductivity at zero concentration was observed to be nearly identical. This fact is illustrated in Table IX which is taken from "Affinitätsmessungen an Schwachen Sauren und Basen" by H. Lunden.

Table IX.

Number of atoms in the acid.	0°	10°	15°	18°	25°	35°	40°	50°
12	241	299	328	344	383	436	463	513
15	239	297	325	342	380	433	460	509
18	238	295	323	340	378	431	457	506
22	237	294	322	338	376	428	455	504
25	236	293	321	337	375	427	454	502
30	235	292	320	336	374	426	452	501

Since β -phenylpropionic acid contains 21 atoms in its molecule, it should have a conductivity of 376.5 at 25°. This is as close an agreement as one could reasonably expect.

The Application of the Correction for the Specific Conductance of the Conductivity Water. In his accurate work on acetic acid, Kendall¹, found that better values for the ionization constant could be obtained by not correcting the conductivity data for the specific

conductance of the water used, provided that the water did not have a specific conductance greater than 0.9×10^{-6} . Whether or not this correction should be applied, seems to depend upon the nature of the impurity in the water. Derick, has demonstrated that calculated Λ_0 gives criterion for determining whether or not the water correction should be applied. The method consists in simply calculating the Λ_0 using the corrected and the uncorrected values for Λ and comparing the values so obtained with the value gotten by the salt method.

In Tables IV, VI and VII are found the values of Λ_0 calculated from the corrected data. It is clear from this data, that for phenylacetic, β phenylpropionic and for propionic acids, the correction should not be applied. The nature of the impurity in the acid measured is a far more important factor to consider than the conductance of the water used; provided that the water is better than 0.9×10^{-6} .

Calculation of the Place Influence of the Phenyl Radical.

The place factors for the phenyl radical in the $\alpha, \beta, \gamma, \delta$ etc. positions are calculated according to Derick's method which follows:

"The influence of all the atoms in the molecule upon the carboxyl in position (1) is defined as proportional to $\frac{1}{\log K}$. It is assumed that this factor is made up additively of the factors of each atom in the molecule. The ratio for these combined influences for the substituted acid to that of the unsubstituted acid is determined. To find the combined direct and indirect influences of the substituent for a given position, the combined influence of the rest of the atoms in the molecule is taken equal to unity, thereby neglecting the value for the hydrogen atom replaced, which occurs additively and is a very small value. This result follows from the fact that in the above ratio the influence of all the atoms in the molecule of the unsubstituted acid is unity, since it occurs in the denominator."

The factor for the phenyl radical would be equal to

$$\frac{1}{\log k \text{ (Substituted acid)}} \div \frac{1}{\log k \text{ (Unsubstituted acid)}} = 1.$$

The following values for the ionization constants are used in the calculations of the α and β factors for the phenyl radical:

	k	10 - log k
Acetic acid	1.850×10^{-5}	-4.73283
Propionic acid	1.415×10^{-6}	-4.84912
Phenylacetic acid	5.171×10^{-5}	-4.28643
α Phenylpropionic acid	4.25×10^{-5}	-4.37161
β Phenylpropionic acid	2.269×10^{-5}	-4.64417

The value for α phenylpropionic acid is that determined by Ostwald, and without doubt has not been determined with the same degree of accuracy as have the others.

The α factor	$\frac{-4.75283}{-4.28643}$	-	.1041	(Using the values for acetic and phenylacetic acids)
The α factor	$\frac{-4.84912}{-4.37161}$	-	.1092	(Using the values for propionic and α phenylpropionic acids.)
The α factor	$\frac{-4.84912}{-4.28643}$	-	.1312	(Using the values for propionic and phenylacetic acids.)
The β factor	$\frac{-4.84912}{-4.64417}$	-	.0441	(Using the values for propionic and β phenylpropionic acids.)

Therefore:

	:	:	:: .1041	:	.0441	:	1	:	$\frac{1}{2.36}$
	:	:	:	:	:	:	:	:	
or	:	:	:: .1092	:	.0441	:	1	:	$\frac{1}{2.47}$
	:	:	:	:	:	:	:	:	
or	:	:	:: .1312	:	.0441	:	1	:	$\frac{1}{2.99}$

depending on the values selected.

The rule of thirds is more nearly approached when propionic and phenylacetic acid are used in the calculation of the α factor. It is unfortunate that the data for the homologues of these acids have not been measured with the required accuracy. But whether or not the rule of thirds holds closely; it appears to be sufficiently approximated to offer a valuable means for determining structure from ionization constants.

IV EXPERIMENTAL (I).

Preparation of β Phenylpropionic acid. An attempt was at first made to use the 'C. P.' hydrocinnamic acid sold by Kahlbaum. A specimen of this was crystallized from logorine (B.p. 78°). The crystals were filtered with suction, washed with a small amount of the solvent, centrifuged, washed as before and again centrifuged for fifteen minutes.* The product was finally dried in a dessicator. The melting point was found to be 46.5° . (Melting points were always taken by the open beaker method.) The conductivity of the acid was finally measured and Λ .calculated. The results were entirely unsatisfactory.

A second sample of the Kahlbaum acid was fractionally crystallized from conductivity water. Fractions melting at 47.5° , 46.5° , 46.5° and 46.5° were obtained. As in the first case the crystals were carefully washed with the solvent and centrifuged, and finally dried in a dessicator. Conductivity measurements were made on each set of crystals, but the results were little better than before. Several sets of measurements were taken on each fraction to make sure that there was no error in manipulation. In all cases a steady drop in the value of calculated Λ .occured. This was taken to indicate the presence of impurities affecting the conductivity of the solutions.

* The electric centrifuge offers a much more efficient method for separating crystals from the mother liquor than the ordinary suction pump. A surprisingly large amount of solvent can be removed by centrifuging crystals apparently dried by suction.

If the hydrocinnamic acid had been made from cinnamic acid by reduction, according to the usual method, one would look for cinnamic acid and possibly benzoic acid as impurities. The latter compound would be extremely difficult to remove and should affect the ionization constant to a very marked degree. The samples of acid used were tested with permanganate solution for unsaturation, but with negative results.

It now seemed best to synthesize the acid to be used for the measurements. For the reason assigned above, the reduction of cinnamic acid was not resorted to. It was finally decided to make use of the malonic ester synthesis. The great advantage of this method lies in the fact that the intermediate products of the reaction can be easily separated and purified.

The synthesis was carried out in the usual manner, but with additional precautions taken to procure pure intermediate products. The calculated amount, 9.2 grams, of sodium was dissolved in sufficient absolute alcohol to keep the resulting sodium alcoholate in solution. To this solution, cooled, was added 64 grams of purified malonic ester. Next 50.5 grams of redistilled benzyl chloride were added thru the condenser. The mixture was now heated on the water-bath, under the reflux, for five hours. The alcohol was next distilled off and water added to the residue. The solution was extracted with ether twice, and the ether extract dried over fused sodium sulphate. The following day the ether was distilled off and the residue fractionated under diminished pressure. The following fractions were obtained:

Fraction 1. Pressure 12mm. Temperature, up to 125°. Weight of fraction 18 grams. Mostly unchanged malonic ester.

Fraction 2. Pressure 25mm. Temperature, 130° to 170°.
Amount, 2.5 cc.

Fraction 3. Pressure 20mm. Temperature, 175° to 193°.
Amount, 33grams. Benzylmalonic ester.

Residue. Weight 29grams. Dibenzylmalonic ester.

It is essential that the temperature be kept low during the addition of the sodium alcoholate to the malon~~st~~ ester, otherwise disodium malonate is formed, due to the hydrolysis of the ester.

The benzylmalonic ester obtained in fraction 3 was redistilled and the portion going over from 172° to 175°, at a pressure of 19mm. to 20mm., was taken for the synthesis of the acid.

The ester was saponified, according to the usual method, using a solution of one part water to three parts potassium hydroxide. After saponification the acid was liberated with hydrochloric acid and the solution extracted with ether, and the ether extract dried over sodiumsulphate. After distilling off the ether the residue was heated to 115°, at which temperature carbon-dioxide began to come off. On cooling a white crystalline mass separated. The mixture was centrifuged to separate the crystals from the liquid. 16 grams of crystals and 19 grams of liquid were thus obtained.

The white crystals were next placed in a distilling bulb and heated until the carbon-dioxide ceased to come off, after which the residue was distilled under diminished pressure. The portion coming over at a temperature of 164° and a pressure of 19mm. was saved. A portion of this was used in making a set of conductivity measurements, and the balance redistilled. This last distillate came over at 170° under a pressure of 26mm. Both distillates melted at 47.5°. The temperature of the second distillate could not be accurately observed on account of violent bumping. The distillates

were finally placed in the weighing tube and kept in a dessicator for the conductivity measurements.

Preparation of the Sodium Salt of Phenylpropionic Acid. The

19 grams of liquid obtained in the synthesis of the benzylmalonic acid, discussed above, were heated under a reflux until all the carbon-dioxide was eliminated; the temperature being finally raised to 150 . The solid residue obtained on cooling was fractionally distilled, and that portion, going over between 165° and 170° at 23mm. pressure, was reserved. This melted at 40° - 48°. This product was redistilled and the fraction distilling between 164° and 165°, at 20mm. pressure, was taken for the preparation of the sodium salt.

The acid obtained as described above was dissolved in a very small amount of absolute alcohol and added to a little less than the theoretical amount of freshly prepared sodium alcoholate. The solution was evaporated until a considerable amount of a curdy precipitate separated. This precipitate was then centrifuged and redissolved in a small volume of absolute alcohol. The solution so obtained was evaporated to a small volume and the curdy precipitate separating was again centrifuged and finally dried in a dessicator. This salt was considered sufficiently pure for the conductivity measurements.

Studies of the Synthesis of γ Phenylbutyric Acid. Having

prepared and measured β phenylpropionic acid, the next problem was make a pure γ phenylbutyric acid. Several syntheses were suggested and tried. Altho these were not successful, they were considered to be of sufficient interest to merit description.

(a) Condensation of Benzyl Chloride and β Iodopropionic Ester

by the Wurtz Method. An attempt was made to condense benzyl chloride with β iodopropionic ester by means of metallic sodium. In this case the possible reactions to consider are the following:

1. $\text{C}_6\text{H}_5\text{CH}_2\text{Cl} + 2\text{Na} \rightarrow [\text{C}_6\text{H}_5\text{CH}_2\text{Na}] + \text{NaCl}.$
2. $\text{ICH}_2\text{CH}_2\text{C}(=\text{O})\text{OR} + 2\text{Na} \rightarrow [\text{NaCH}_2\text{CH}_2\text{C}(=\text{O})\text{OR}] + \text{NaI}$
3. $\text{C}_6\text{H}_5\text{CH}_2\text{Cl} + [\text{NaCH}_2\text{CH}_2\text{C}(=\text{O})\text{OR}] \rightarrow \text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{CH}_2\text{C}(=\text{O})\text{OR} + \text{NaCl}$
4. $[\text{C}_6\text{H}_5\text{CH}_2\text{Na}] + \text{ICH}_2\text{CH}_2\text{C}(=\text{O})\text{OR} \rightarrow \text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{CH}_2\text{C}(=\text{O})\text{OR} + \text{NaI}$
5. $[\text{C}_6\text{H}_5\text{CH}_2\text{Na}] + \text{ClCH}_2\text{C}_6\text{H}_5 \rightarrow \text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{C}_6\text{H}_5 + \text{NaCl}$
6. $\text{ICH}_2\text{CH}_2\text{C}(=\text{O})\text{OR} + [\text{NaCH}_2\text{CH}_2\text{C}(=\text{O})\text{OR}] \rightarrow \begin{array}{c} \text{CH}_2\text{CH}_2\text{C}(=\text{O})\text{OR} \\ | \\ \text{CH}_2\text{CH}_2\text{C}(=\text{O})\text{OR} \end{array} + \text{NaI}$
7. $\text{ICH}_2\text{CH}_2\text{C}(=\text{O})\text{OR} \rightarrow \text{CH}_2=\text{CH}_2\text{C}(=\text{O})\text{OR} + \text{HI}.$

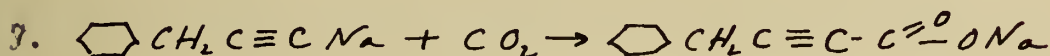
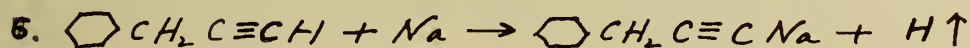
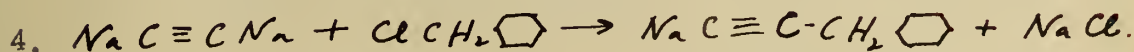
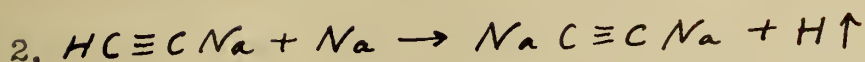
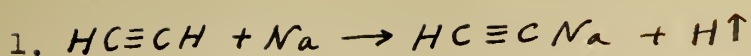
The compounds enclosed in brackets are those theoretically possible, but not isolated in the course of the reaction.

It can be seen that the desired product is obtained by either reaction 3 or 4. The relative speed of 1 and 2 will determine the importance of 3 or 4 in producing the ester. Reactions 5 and 6 yield the byproducts, sym-diphenylethane and adipic ester respectively. Here again, the amounts of substance formed will depend largely upon the relative speeds of 5 and 6. Acrylic ester is formed according to equation 7, the amount depending upon the speed of the reaction.

Unfortunately, little is at present known concerning reaction velocities. If it were otherwise one could control the yields of the various products by regulating the masses of substances used. As it is, one must determine by experiment the amounts of reagents that are the most advantageous to use.

In order to test the method, the following experiment was tried: 17 grams of β -iodopropionic ester (recrystallized from acetone) were dissolved in 100cc. of absolute ether in a 500cc. round-bottom flask. To this was added 4 grams of sodium and 10 grams of redistilled benzyl chloride. A reflux condenser was attached to the flask and the ether solution boiled for a short time and finally allowed to stand over night. The following day the straw colored solution was poured from the residue of salt and undecomposed sodium. The residue was washed with ether and the washings combined with the main solution. The ether was distilled off and the 25cc. of liquid remaining were fractionated. The greater part of the liquid distilled between 170° and 185° . Above 195° there was a decided decomposition, free iodine being evolved. Only a few drops of the substance distilled above 200° . The main portion of the distillate did not prove to be phenylbutyric ester. Evidently the conditions were not properly regulated for the success of the method. It would probably have been better to have used benzyl bromide rather than the chloride. However, it did not seem advisable to continue the further study of this synthesis, on account of the high cost of materials and because of the number of byproducts of the reaction.

(b) Condensation of Sodium Acetylides and Benzyl Bromide. A second synthesis was suggested in which sodium acetylide was to be condensed with benzyl bromide, and the resulting benzyl acetylide converted into its sodium derivative. This compound suspended in dry ether and treated with carbon-dioxide should yield phenyltetrolonic acid, $\text{C}_6\text{H}_5\text{CH}_2\text{C}\equiv\text{CC}(\text{O})\text{Na}$, which on reduction ought to give the desired γ -phenylbutyric acid. The following reactions come under consideration:



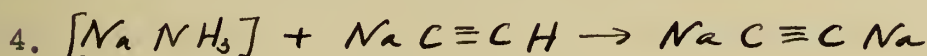
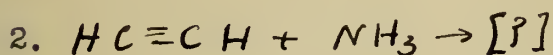
Reactions 1, 3, 6, and 7 are the ones desired. An excess of sodium favors 2, and consequently 4 and 5. An excess of acetylene favors 1. Hence, an excess of acetylene should be used.

The sodium was placed in a round-bottom flask and a stream of acetylene, purified by passing thru potassium hydroxide and mercuric chloride solutions, and finally dried by passing over calcium chloride, was passed over the sodium. When all the air in the flask had been displaced by acetylene the flask was heated slowly from 120° to 180° while a steady stream of acetylene passed over the melted sodium. The flask was shaken from time to time to allow the gas to come in contact with as large a surface of sodium as possible.

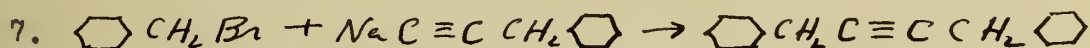
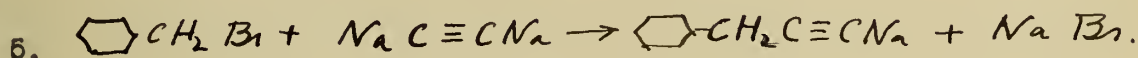
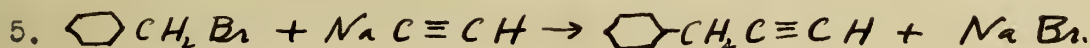
The resulting gray powder could not be made to react with benzyl chloride in ether solution. This was possibly on account of the insolubility of the powder in the ether. On heating the mixture of the dry powder and benzyl chloride, after driving off the ether, a reaction was brought about resulting in the decomposition of the substances with the liberation of carbon. This may have been due to

the excess of sodium present.

Since pure sodium acetylide could not be prepared in the manner described above, its synthesis in liquid ammonia was next tried. The following possibilities are to be considered:



By always keeping present a large excess of acetylene, reaction 4 would be suppressed. The method by which this was accomplished will be described below. After the formation of the sodium acetylide, benzyl bromide was dropped into the solution. Here the following reactions probably take place:



If reaction 4 has been suppressed, 6 and 7 need not be considered.

The apparatus for this synthesis was arranged as follows: Liquid ammonia was placed in a silvered Dewar flask of about one pint capacity. Dry sodium was slowly dropped into this until the amount calculated for the synthesis was added. The solution soon turned a deep blue color. Sufficient liquid ammonia was present to form a mobile liquid. This flask was then fitted with a three-hole rubber stopper. Thru one hole passed a safety tube. Thru the second,

passed a tube leading to a hydrogen generator. The third hole carried a glass tube of 5mm. diameter, running nearly to the bottom of the flask. This tube connected the first Dewar flask with a second, which was unsilvered, and which contained liquid ammonia saturated with acetylene. The air in the first Dewar flask was displaced by an atmosphere of hydrogen, and that in the second by an atmosphere of acetylene. By opening the valve between the hydrogen generator and the first flask, the pressure on the surface of the sodium-ammonia solution forced the solution thru the tube into the second flask. The deep indigo color of the sodium solution immediately disappeared on coming in contact with the acetylene solution. The sodium solution was thus forced over, a little at a time, until the flask was emptied. During this process a rapid stream of acetylene passed continually thru the ammonia, in order to insure saturation with the gas.

Benzyl bromide was next added drop by drop to the sodium acetylide solution, in the amount calculated to react with the latter compound. At first no change could be observed, but soon the solution assumed a yellowish color and an oil collected at the bottom of the flask. Finally the contents of the flask assumed a salmon color and a white precipitate settled out, the oil having disappeared. When the reaction seemed to be complete the mixture was poured into a porcelain dish and the ammonia allowed to evaporate. The residue was extracted with anhydrous ether and the extract set aside; (Extract 1). A second extraction was made using moist ether, (Extract 2). At last the remaining solid was dissolved in water, when an oil separated. This was extracted with ether and dried over sodium sulphate, (Extract 3).

On distillation these ether extracts yielded straw colored liquids which had very high boiling points and became viscous after heating. None of these residues resembled the desired product. It was thot that they were polymerization products. Lack of time prevented a more extended investigation of thses substances.

(c) Styrolene Bromide and Malonic Ester. If styrolene bromide could be made to condense with malonic ester, the resulting condensation product on saponification and elimination of carbon-dioxide should give 4-phenyl- butanoic acid. This compound upon seduction would yield γ phenylbutyric acid.

The styrolene bromide was prepared by the method of Nef¹⁹. Then the usual precautions for the malonic ester condensation were taken, but the styrolene bromide could not be made to condense with the ester even after six hours heating. Altho some sodium bromide separated, most of the ester was recðvored unchanged.

Styrðlene Bromide and Chloroacetic ester. The following experiment was tried to see if styrolene bromide could be made to condense with chloroacetic ester, by the Grignard method:

12.2 grams of chloroacetic ester, which had been dried over calcium chloride and distilled, were dissolved in 20cc. of absolute ether. 2.4 grams of carefully cleaned magnesium ribbon were added and the whole boiled in a round-bottom flask under a reflux. A small crystal of iodine was added thru the top of the condenser to start the reaction. Soon all but a few fragments of the magnesium ribbon had dissolved. When the reaction had apparently ceased 18.3 grams of styrolene bromide in 25cc. of dry ether were added and the mixture boiled for three quarters of an hour. Next the ether was

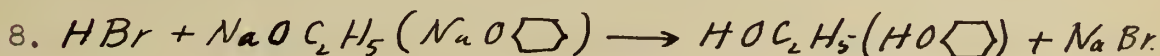
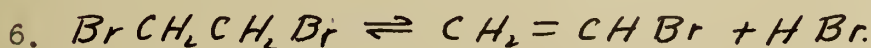
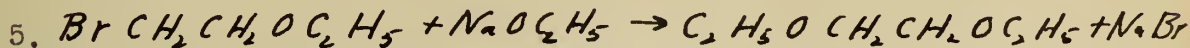
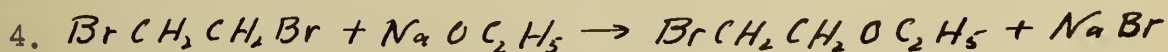
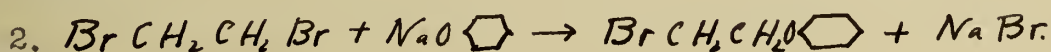
distilled off and the brownish liquid remaining was decomposed with a 10 per cent solution of hydrochloric acid, during which the reaction mixture was kept well cooled. An oily brown layer separated which was extracted with ether and dried a few minutes over anhydrous potassium carbonate, and finally over sodium sulphate. The ether was distilled off and the residue distilled under diminished pressure. At 35mm. most of the product distilled, the temperature rising from 105° to 115°. Yield 11 grams. The substance so obtained was treated with 20 per cent potassium hydroxide solution to saponify the ester, if present. The mixture was heated for six hours on the water bath. The contents of the flask were acidified with hydrochloric acid and the solution extracted with ether. After drying over sodium sulphate and distilling off the ether, only a few drops of liquid remained. It was not considered worth while to experiment further with this condensation.

(d) Preparation of 1-Phenyl,2-iodoethane. Since styrolene bromide could not be made to condense with malonic ester, it was found necessary to prepare the corresponding saturated compound. There should be no difficulty in condensing bromophenylethane or phenyl-iodo ethane with the ester. The starting point for this synthesis was ethylene bromide. This was to be converted into 1-phenoxy-2-bromethane. This compound, by the Grignard method, could be converted into 1-phenoxy,2-phenylethane. The latter compound treated with hydroiodic acid should give 1-phenyl,2-iodoethane, $\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{I}$.

Preparation of 1-phenoxy,2-bromoethane. 11.5 grams of sodium were dissolved in absolute alcohol and placed in a 750cc. round-bottom flask, thru the stopper of which passed the tube of a reflux condenser. Thru another hole in the stopper of the flask

passed the stem of a dropping funnel. A series of U-tubes were connected with the top of the condenser. The first two of these contained absolute alcohol and were cooled in ice water. The vinyl bromide liberated in the course of the reaction was absorbed in these tubes. A third U-tube was empty and acted as a safety, and a fourth contained a few grams of bromine to absorb the acetylene.

When the sodium had entirely dissolved in the alcohol in the flask, a cooled solution of 47 grams of phenol in alcohol was added. The mixture of sodium phenolate - sodium alcoholate was now placed in the dropping funnel. In the flask was placed 188 grams of ethylene bromide. The ethylene bromide was brought to the boiling point and the sodium phenolate-alcoholate mixture added drop by drop to the boiling bromide. The addition of the mixture required about one hour and a half. The following reactions are to be considered:



Experience has shown that the equilibrium indicated in

reaction 1 is attained when a large excess of sodium phenolate is formed. This excess of sodium phenolate over sodium alcoholate favors reactions 2 and 3, and surpresses 4 and 5. The amounts of bromophenoxyethane and diphenoxyethane formed will depend upon the relative amounts of sodiumphenolate and ethylene bromide present, as well as the relative velocities of reactions 2 and 3. The method of addition of sodium phenolate insures a large excess of ethylene bromide and therefore favors reaction 2.

In absolute alcohol ethylene bromide disso~~ci~~ates, to a limited extent, yielding vinyl bromide and hydrobromic acid. Vinyl bromide is further disso~~bi~~ttiated into acetylene and hydrobromic acid. Under ordinary conditions equilibrium is attained when a very small amount of hydrobromic acid is formed. However, in the presence of sodium alcoholate or other basic substance, the hydrobromic acid is removed from the field of action and the yield of vinyl bromide and acetylene is thereby increased. The proportion of vinyl bromide formed will ~~d~~epend upon the relative amounts of sodium alcoholate and ethylene bromide present. With an excess of alcoholate the acetylene is the main product. With an excess of ethylene bromide, vinyl bromide is the principal product. The relative amounts of vinyl bromide and ether formed will depend upon the reaction velocities and can not be controlled by mass action. In all experiments tried there was a considerable amount of vinyl bromide formed and a little acetylene.

After all the alcoholate-phenolate mixture had been added the contents of the flask were boiled for an hour and a half longer. The sodium bromide was then filtered off with suction and washed with a little absolute alcohol. The excess of alcohol was driven off from the filterate and the residue distilled - the temperature being

raised to 150°. The portion going over up to 150° consisted, for the most part, of unchanged ethylene bromide. The residue from this distillation was then fractionated under diminished pressure.

Fraction 1. Pressure, 35-20mm. Temp., 87°-100°. Weight, 45grams.

Fraction 2. " 21 " " 114°-120° " 4 "

Fraction 3. " 21-22 " 117°-132° " 23 .

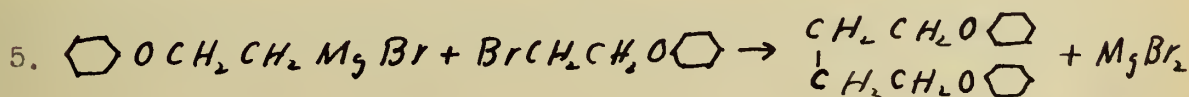
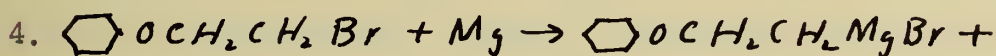
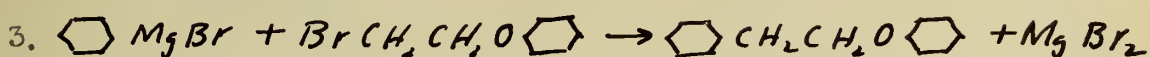
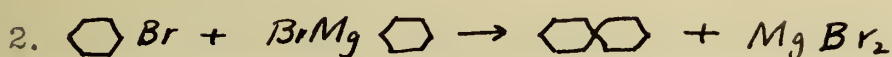
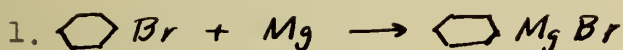
The small amount of residue was discarded.

A second preparation was made as described above and fractionated. Fractions 1, 2 and 3 from both experiments were combined and redistilled. Finally, 48 grams of nearly pure phenoxybromoethane corresponding to fraction 3, was obtained. This product was used without further purification for the next step in the synthesis.

Condensation of Phenoxybromoethane with Magnesiumphenylbromide. 6 grams of carefully cleaned magnesium ribbon were placed in a 500cc. flask, under a reflux condenser. Thru the top of the condenser was added 40 grams of pure dry bromobenzene and 10cc. of absolute ether, to which had been added a little powdered iodine. A very vigorous reaction set in and 40cc. more ether was added in 10cc. portions to moderate this. Finally the flask had to be cooled in ice water. After about half an hour the mixture was heated on the electric heater and the heating continued for an hour. By this time nearly all of the magnesium had disappeared. The excess of ether was next distilled off and the 48 grams of phenoxybromoethane, $\text{C}_6\text{H}_5\text{OCH}_2\text{CH}_2\text{Br}$, mixed with 50cc. of phenetole, were added. 1cc. of dimethyl aniline was added to the mixture to catalize the reaction. The flask was heated for a short time and allowed to stand over night. By this time the contents of the flask had assumed a gray color. When the phenetole solution was heated the ether was, of

course, driven off and the temperature considerably raised. The following morning two volumes of water were added. An oil separated and a flesh-colored solid appeared on the bottom of the flask. The mixture was distilled with steam to remove the oil - phenetole. Finally, the contents on the flask, after being cooled, were acidified with dilute sulphuric acid. The resulting oil was separated and the aqueous layer extracted with ether. The extract and oil combined were dried over sodium sulphate and the ether distilled off. The residue was fractionated, and the fraction distilling between 150° and 175° , at 20mm. pressure, reserved. This consisted of the desired phenoxyphenylethane. Yield 14.4 grams.

The following reactions may take place during the course of the experiment:



It has been found that the production of diphenyl, indicated in reaction 2, is not an important factor under the conditions of the experiment, when there is sufficient magnesium to react with the bromobenzene. Evidently the velocity of 1 is much greater than 2.

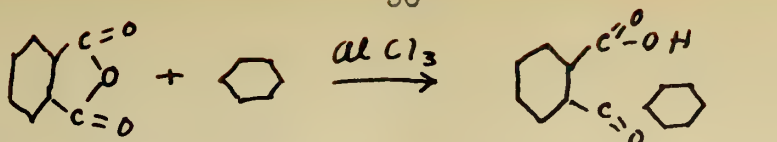
If a large excess of magnesium is not present, reaction 4 is relatively unimportant. Consequently, 5 and 6 need not be

considered. In order to complete reaction 5 it is necessary to work at a higher temperature than is possible in ether solution. For this reason phenetole is added to displace the ether.

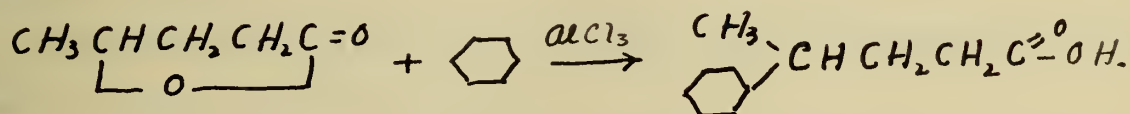
Replacement of the Phenoxy Group by Iodine. The 14.4 grams of phenoxyphenylthane, obtained as described above, were mixed with two volumes of hydroiodic acid, sp. gr. 1.96, and placed in a small flask attached to a reflux condenser by a ground glass stopper. The contents of the flask were heated on the Wood's metal bath for two hours at a temperature varying from 111° to 135°. After cooling, water was added, which caused an oil to separate. The aqueous layer was neutralized with 1:1 potassium hydroxide and extracted with ether. This was combined with the oil and dried over sodium sulphate, after which the ether was distilled off. The residue was next distilled with steam to separate the volatile phenylethyl iodide from the non-volatile phenoxyphenylthane.

The oily layer was then separated from the distillate and the aqueous layer extracted with ether. The extract and oil were dried, as usual, over sodium sulphate. The ether was distilled off and the residue fractionated. A product weighing 4.6 grams was obtained which distilled between 130° and 142° under 25mm. pressure. There was a very marked decomposition during the distillation, iodine being liberated. It was not considered prudent to use this product in the synthesis of the acid.

(e) Condensation of Benzene and Butyrolactone by Friedel and Crafts' Method. It is well known that benzene can be condensed with certain aromatic anhydrides, such as phthalic anhydride, by means of aluminium chloride.

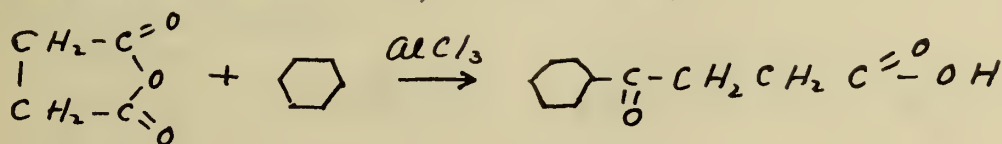


Eijkman₂₁ found that aliphatic anhydrides and lactones would condense in a similar fashion. For example, he obtained methylphenylbutyric acid from methylbutyrolactone as shown in the following reaction:

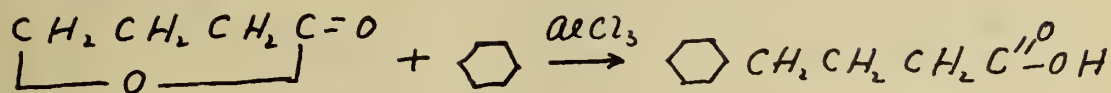


In order to test Eijkman's method the following experiment was tried:

60 grams of succinic anhydride were dissolved in 600cc. of benzene. To this was added 90 grams of anhydrous aluminium chloride. A yellowish solid formed at once with but little evolution of hydrochloric acid. A reflux condenser, closed at the top by means of a stopper bearing a calcium chloride tube, was attached to the flask and the mixture allowed to stand for four days. At the expiration of this period the contents of the flask were poured into an excess of water and hydrochloric acid was added with cooling, to liberate the acid from its aluminium salt. A yellow precipitate separated which was filtered off with suction. The benzene solution was next extracted with potassium hydroxide solution and the extract treated with hydrochloric acid. A second crop of the yellow crystals was thus obtained which was combined with the first and the whole recrystallized from benzene. 57 grams of this compound, benzoylpropionic acid, were obtained, corresponding to a yield of 50 per cent. The substance melted at 114° , uncorrected.

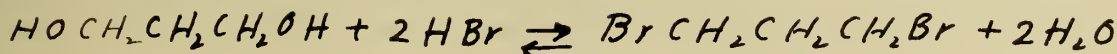


It was now considered feasible to condense benzene with butyrolactone by this method.

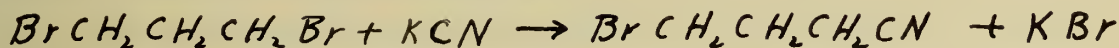


In order to prepare pure butyrolactone the following synthesis was tried:

Trimethyleneglycol was converted into trimethylene bromide by means of 48% hydrobromic acid.



The trimethylene bromide was next treated with potassium cyanide to convert it into the bromonitrile.



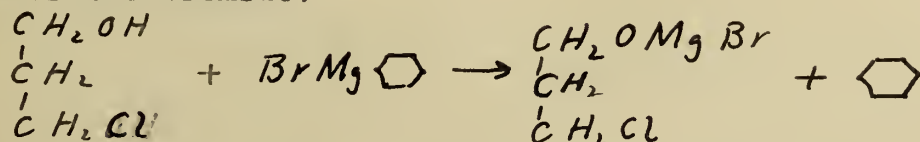
(The details of the two steps mentioned above were worked out by Derick and Hess₂₂) The yields were very good in both cases.

Upon saponification, the nitrile should yield either bromobutyric acid or the lactone directly. A number of attempts were made to saponify the nitrile but in all cases small yields of impure material were obtained and the method had to be abandoned.

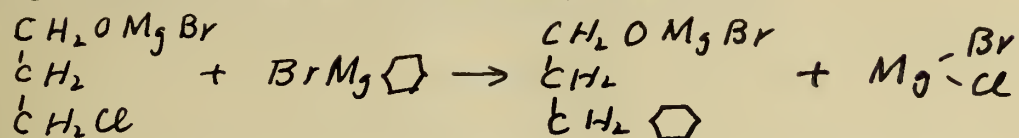
(f) Synthesis of 1-bromo, 3-phenylpropane, $\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{CH}_2\text{Br}$.

This compound could be used for the preparation of either γ -phenylbutyric acid or δ -phenylvalerianic acid.

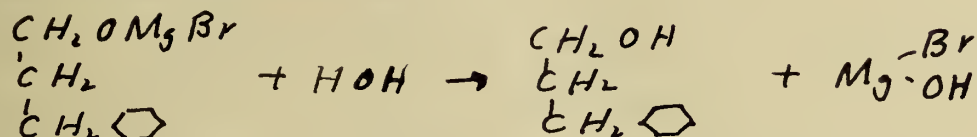
The starting point of the synthesis is trimethyleneglycol. This substance treated with sulphur monochloride will yield trimethylenechlorhydrine, $\text{HOCH}_2\text{CH}_2\text{CH}_2\text{Cl}$. Trimethylenechlorhydrine treated with magnesium phenylbromide reacts as follows with one molecule of the bromide:



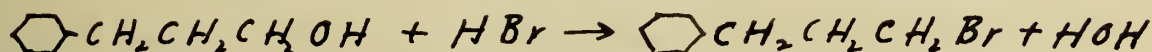
A second molecule of the magnesium phenylbromide will then react, replacing the chlorine with the phenyl radical:



If the mixture is then treated with water the alcohol will be formed according to the reaction₂₃,



The alcohol can then be treated with 48% hydrobromic acid to replace the hydroxyl group by bromine.



The synthesis described above is now being studied.

V EXPERIMENTAL (II).

(Apparatus.)

The Balance. A very sensitive analytical balance, having divisions reading to 0.05 mg. on the rider arm, was used. This instrument remained accurately adjusted thruout the course of the experiments. The zero point would shift but slightly during the lapse of several months.

The Weights. The larger weights were of brass and were gold-plated, the smaller ones were of platinum. The set had been carefully calibrated in the laboratory by the well known method of Richards. This calibration was checked by The Bureau of Standards. In all weighings the corrections were applied.

The Cells. Two cells of the pipette form were used. These cells were made of resistance glass and had been steamed out for several hours. When not in use they were always filled with conductivity water. The cell constants were determined by the method of Kohlrausch₂₄. The conductivity of a 1/50 N. potassium chloride solution was measured in the cell, then the conductivity of a 1/100 N. solution. The constant was then calculated from the formula $C = \frac{L}{L}$,

A fuller discussion of the apparatus used, and a discussion of the methods of calibrating the bridge, box and the weights may be found in a Master's Thesis by Anton Prasil, University of Illinois, 1914.

in which C is the cell constant, κ the conductivity of the solution given in Kohlrausch's tables, and L the measured conductance of the solution. The potassium chloride was purified by recrystallization several times, and finally fused and pulverized.

Two types of cells were used. One was a water cell having electrodes 2cm. in diameter and $1\frac{1}{2}$ mm. apart. The capacity of this cell was about 25cc. This cell was used in measuring the conductivity of the water and the very dilute solutions. The second cell had platinized electrodes 12mm. in diameter and $1\frac{1}{2}$ mm. apart. The capacity was about 15cc.

A third cell of the same form as the one described above but having unplatinized electrodes was tried. But it was not possible to get as sharp endpoints on the bridge with this as with the platinized cell; and its use was discontinued.

The Bridge. A Kohlrausch bridge of the form described in the Leed's and Northrup catalog No. 48 was used. This consists of a \propto bridge wire mounted on a marble cylinder 15 cm. in diameter. The wire is covered by a protecting hood on the inside of which is the sliding contact. The hood revolves upon a threaded spindle. The position of the contact is read by means of a vertical glass scale each division of which corresponds to one complete turn of the hood. Around the periphery of the hood is a second scale divided into 200 parts to record the fractions of a turn. By means of these subdivisions it is easily possible to estimate to a thousandths of a revolution which correspond to ten-thousandths of the total length of the wire.

Resistance Box. A decade resistance box reading to 10,000 ohms was used. This box was calibrated and the readings were always

corrected when the correction would amount to one tenth of one per cent or over. In most cases, however, the correction was too small to be applied.

Telephone and Vibrator. The source of E.M.F. was a small induction coil activated by dry cells. It has been pointed out that for very accurate conductivity work the induction coil should be discarded. It is not possible to hold the frequency constant, so that the advantage of a tuned telephone receiver is lost. Furthermore the current is a pulsating, more than alternating current. This leads to considerable polarization in the cell. But since an accuracy of not more than one tenth of one per cent was aimed at, it was not deemed necessary to use more refined instruments. As long as chemicals are used which contain unavoidable impurities there seems little reason for developing the technique of physical measurements to a great extent. This applies to the chemist with more force than to the physicist.

Thermostat. On account of the high temperature coefficient of resistance of electrolytes, it is necessary to have a very accurate control of the temperature during the measurements. For example, the temperature coefficient for conductivity water is greater than 4% per degree.

The constant temperature bath used in this work consisted of a silvered Dewar flask of about two liters capacity, placed in a large glass jar covered with asbestos. The Dewar was filled with distilled water. Into this dipped a heating coil of Nichrome wire and a glass cooling coil thru which cold water could be made to circulate. A stirrer agitated by a small motor, and a Beckman thermometer completed the equipment. With this apparatus it was found

possible to keep the temperature at $25 \pm .02$.

(Conductivity Water)

Great care had to be taken in the preparation of the conductivity water. The still consisted of a copper tank of about eight gallons capacity. At the top of this was a tower containing baffle plates. From this extended a block tin condenser. The heating device was a steam coil placed within the tank.

Ordinary distilled water to which was added 100cc. of an alkaline permanganate solution was run into the tank and the steam turned on until the water was brought to a boil. The steam was then turned off and the still allowed to stand for from six to twelve hours. After standing, the steam would again be turned on and about one-fourth of the water distilled over. The distillate would then be tested with Nessler's reagent and if found ammonia free the water would be collected. Large bottles of resistance glass were used to preserve the water. These bottles had been in contact with conductivity water for two or three years and were steamed off from time to time.

While collecting the water the end of the condenser would be placed well down in the neck of the bottle and the distillation so regulated that a current of steam continually escaped into the room. This prevented contamination of the water by fumes from the laboratory.

The bottles were closed by folding a piece of wellsteamed tin foil over the mouth. After cooling, if the water was found to have a conductivity greater than 0.9×10^{-6} it would be redistilled. Water prepared as described above usually had a conductance of

from 0.5×10^{-6} to 0.7×10^{-6} . On standing the conductance would increase rapidly at first, and then slowly. Ordinarily, after two or three days, if the bottle had not been opened, the water would be better than 0.85×10^{-6} .

(Method of Making up and Measuring Solutions.)

The acid or salt to be measured was kept in a small weighing tube with a ground glass stopper. This tube after being wiped with a clean linen handkerchief was placed on the pan of the balance with as little handling as possible. It was noticed that in order to get a constant weight it was necessary to allow the tube to stand on the balance pan for ten or fifteen minutes before the final adjustment of the rider was made. The required amount of the acid would next be dropped from the tube into a weighed flat-bottom Jena flask of 500cc. capacity. The tube would then be weighed as before, after the expiration of ten or fifteen minutes. The flasks had been in use in this work for several months and were steamed out from time to time.

Two portions of the acid would be weighed out as indicated and the flasks marked A and B. Next the amount of water necessary to make a 0.01 N solution would be weighed into the flasks on a second balance which was sensitive to 0.05 gram. In order to reduce the error of weighing as much as possible, sufficient acid would be weighed out to make up about 300 grams of solution.

Next the conductivity of the solutions A and B would be measured. This was always done as follows: the conductivity cell would be filled with the solution three times, and emptied. Finally it

would be filled and placed in the thermostat and allowed to remain for fifteen minutes - in the case of the water cell for twenty minutes - to attain the temperature of 25° . After this the stirrer would be stopped and the vibrator started, and sufficient resistance plugged in the box to give a balance at about the middle of the bridge. In taking the readings the current would be turned on by means of a key, a few seconds at a time only. Three readings were always taken, varying the resistance sufficiently to give zero points ten to fifteen divisions apart.

After measuring ~~solution~~ A, B would be measured in a similar fashion. If B was found to have the same conductivity as A, a series of dilutions were made from A and B. If the conductivity of A and B were not close together new solutions were made up and measured until concordant results were obtained.

The dilutions from A and B were made up after the following fashion: About 100 grams of the solution in A would be weighed into a new flask and sufficient water weighed in to make the solution 0.0075 N or 0.0050 N as the case might be. In a similar manner a solution of the same strength would be made from B. These two solutions would then be measured and if found to have practically the same conductivity would be marked A' and B'. The higher dilutions would then be made from these in the same manner as before. If A' and B' did not check new dilutions would be made from A and B.

In this manner a series of dilutions would be made beginning with a 0.01 N solution and continuing down to 0.00010 N. A second series would then be made beginning with the 0.0075 N solution. Then a third beginning with the 0.0050 N solution. It was found expedient to thus make up the 0.01N, 0.0075 N, 0.0050 N, 0.0025 N, and the

0.0010 N solutions by weighing in the acids and to make up the higher dilutions from these.

The phenylpropionic acid is slowly soluble in cold water. It was necessary to add a portion of the conductivity water and then to cover the flask and warm the solution slightly on a water bath until the acid dissolved. After this the flask was again placed on the balance and the remainder of the water necessary for the dilution added. The flasks were usually warmed to 70 or 80 to insure solution. On cooling the acid did not separate.

It was not found possible to get sharp endpoints on the bridge for the 0.00025 N and the 0.00010 N dilutions, using either the platinized or the water cell. It is therefore justifiable to neglect the values for the ionization constants for these dilutions. Table X contains the resistances and the bridge readings for the various dilutions made on the pure sample of β -phenylpropionic acid. The conductance for each dilution was calculated for each of the three readings. Then the average of the three, taken for the conductance at that particular dilution.

The numbers underscored are for dilutions made up directly from a weighed sample of the acid. The others were made up by dilution as previously indicated. The readings designated by an asterisk are the ones used in the calculation of the data given in Table VI. These were selected from the others using calculated Λ_0 as a criterion of accuracy.

The sodium salt was measured in the same way as the acid; except that it was not necessary to warm the solution to dissolve the salt in the first place. The readings are given in Table XI. The extrapolation to Λ_0 was made graphically by the method of Kohlrausch.

by plotting Λ against C . The values 80.13, 79.80, and 79.30 were obtained, the first of these being selected for the calculation of the mobility of the β phenylpropionate ion. Taking the mobility of the sodium ion as 51.2 one obtains the value 28.9 for the negative ion. This added to 247.2, Kendall's value for hydrogen, gives 376.1 for the value of Λ_0 for β phenylpropionic acid. This number was used in calculating the ionization constants.

The curve shown in Plate I was taken from the original plot and has been reduced to one-fourth the actual size by means of a precision pantograph.

Table X.

Conductance Data for β Phenylpropionic Acid.

Dilution. R		Bridge Readings.									
		*									
0.01N	350.02	5028	5028	5027	5028						
	360.03	4957	4957	4957	4957						
	370.02	<u>4892</u>	<u>4890</u>	<u>4887</u>	<u>4888</u>						
		*									
0.0075	400	5065	5065								
	410	5003	5002								
	420	<u>4941</u>	<u>4942</u>								
		*									
0.0050	499.9	5033	5030	5023	5024	5030	5030	5029	5027		
	509.9	4982	4978	4974	4975	4977	4977	4982	4977		
	519.9	<u>4931</u>	4928	4925	4926	4932	4932	<u>4933</u>	<u>4932</u>		
		*									
0.0025	799.9	4757	4757	4756	4757	4757	4759	4762	4862	4756	4754
	809.9	4726	4726	4725	4724	4726	4729	4732	4732	4722	4724
	819.9	4692	4793	4693	4694	4696	4697	4701	4700	<u>4692</u>	<u>4692</u>
		*									
0.0010	1200	4971	4972	4959	4956	4962	4966	4959			
	1220	4928	4930	4918	4915	4923	4925	4920			
	1240	4887	4887	<u>4877</u>	<u>4873</u>	4878	4883	4880			
		*									
0.00075	1400	4969	4972	4972	4972	4978	4979	4963	4864	4966	4966
	1430	4917	4920	4918	4919	4927	4928	4912	4912	4912	4911
	1460	4865	4866	4866	4867	4874	4875	4859	4859	4859	4857
		*									
0.00050	1800	4915	4925	4915	4918	4918	4896	4894			
	1820	4885	4897	4885	4888	4888	4866	4867			
	1840	4859	4872	4858	4862	4862	4839	4836			
0.00025	2500	5067	5070								
	2540	5025	5025								
	2580	4984	4989								
0.00010	5000	4740									
	5300	4590									
	5600	4455									
(Changed to Water Cell)											
		*									
0.00025	799.9	5066	5055	5055	5017	5024					
	819.9	5003	4993	4992	4957	4964					
	829.8	4942	4933	4933	4897	4902					
		*									
0.00010	1500	4880	4904	4839	4805						
	1600	4717	4736	4678	4645						
	1700	<u>4567</u>	4992	4527	4495						

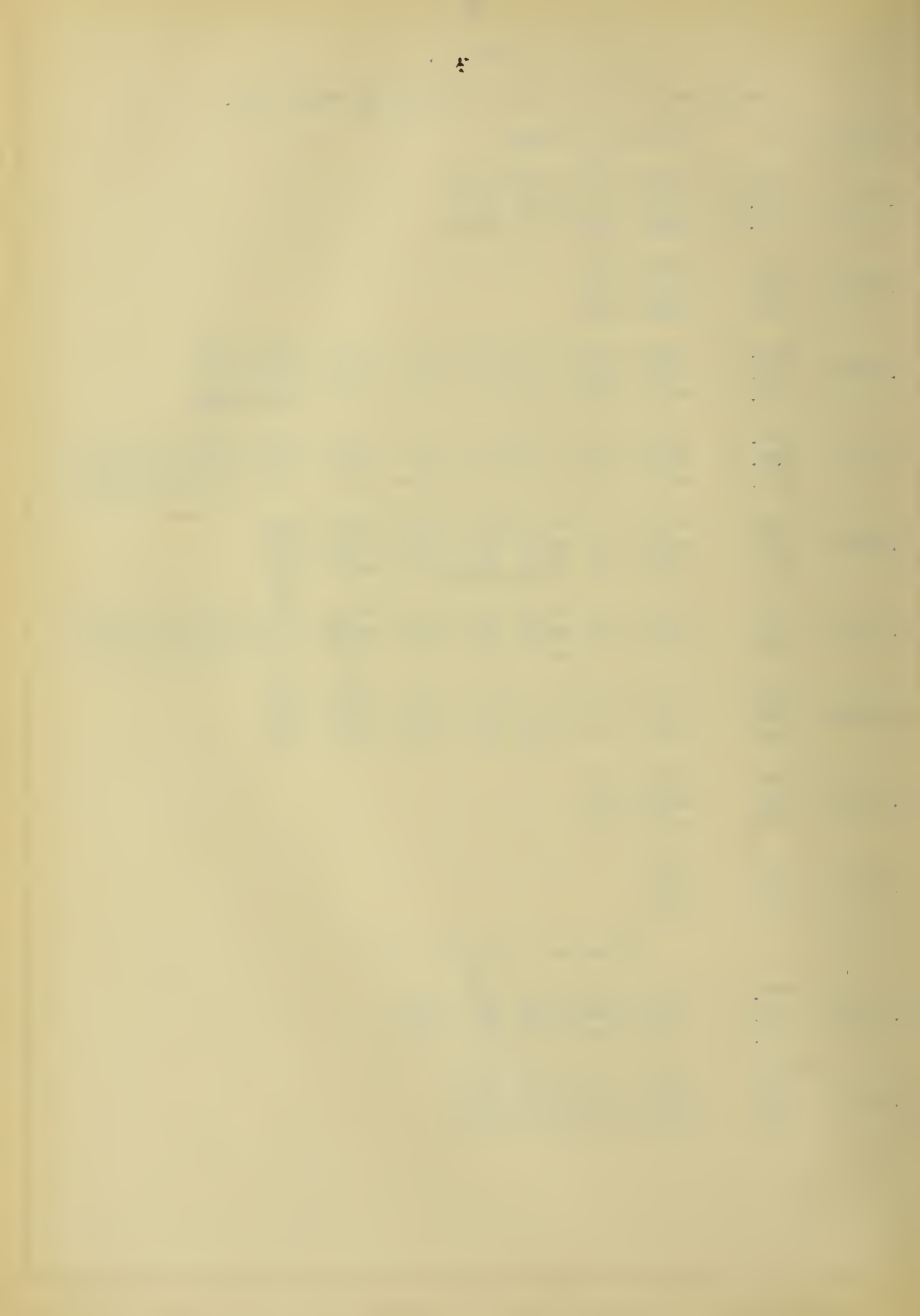


Table XI.

Conductance Data for Sodium Salt of β -Phenylpropionic Acid.

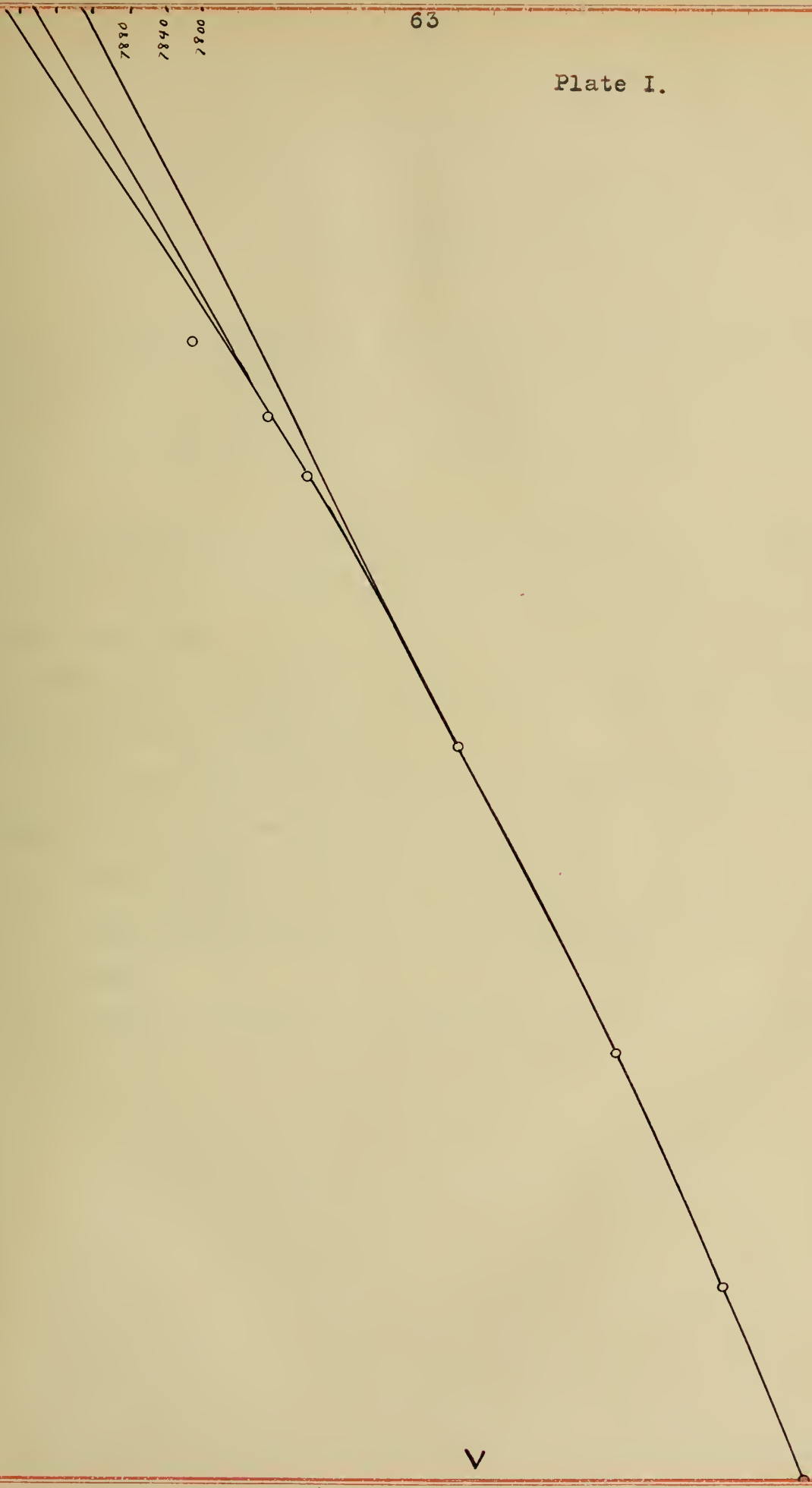
Dilution.	R	Bridge Readings.			
0.01N	90.024	4900	4909		
	92.032	4854	4852		
	94.030	<u>4797</u>	<u>4799</u>		
0.0075	110.01	5093	5089		
	120.00	4874	4874		
	130.00	4675	4674		
0.0050	170.00	4977	4972		
	180.00	4834	4832		
	190.03	4702	4697		
0.0025	330.02	5001	4995	5001	5001
	340.00	4928	4920	4932	4927
	350.02	4853	4849	<u>4854</u>	<u>4852</u>
0.0010	799.86			5017	5021
	819.85			4954	4955
	839.83			4895	4897
0.00075	1100.1			4932	4928
	1120.1			4886	4883
	1140.1			4846	4837
0.00050	1600.1			4976	4977
	1620.1			4946	4947
	1640.1			4915	4917
0.00025	3000.1			5065	5076
	3100.1			4984	4994
	3200.1			4902	4917

Plate I.

 τ_c

V

0001

8040
7880
7840
7800

VI SUMMARY.

1. A critical study of the various hypotheses concerning the relationship of ionization and structure has been made.
2. The scale of influence proposed by Michael has been discredited.
3. Flurscheim's conclusions have been shown to be fallacious.
4. The 'rule of thirds' proposed by Derick has been found to hold approximately.
5. The calculated Λ_0 as a criterion of accuracy in conductance data has been considered.
6. A calculation has been made for the β place influence of the phenyl radical in monobasic paraffine acids.
7. Phenylpropionic acid and its sodium salt have been prepared in a high state of purity and the ionization constant of the acid determined.
8. Various syntheses of phenylbutyric acid have been studied.

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IX BIOGRAPHICAL.

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